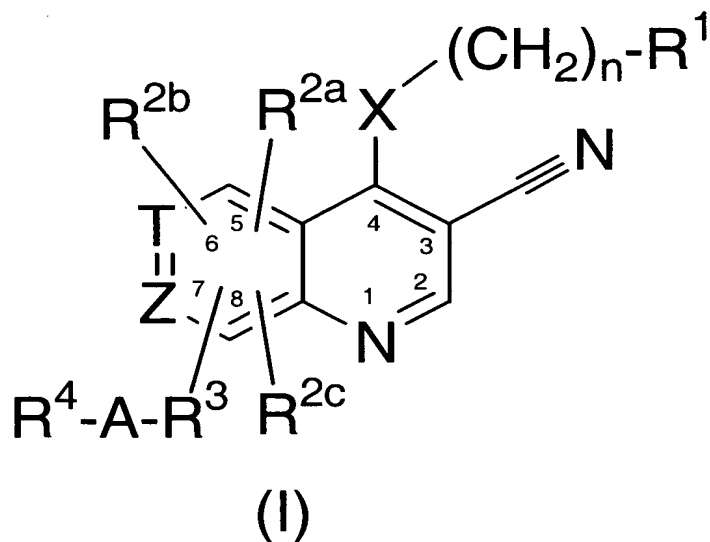


AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A compound of Formula (I) represented by the structure:



wherein:

X is -NH-, -NR⁵-, -O-, or -S(O)_m-;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is -(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -(C(R⁹)₂)_r C(O)-, -cycloalkyl- or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(O)H, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C=C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

a heteroaryl ring having 5 or 6 atoms containing 1 to 4 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

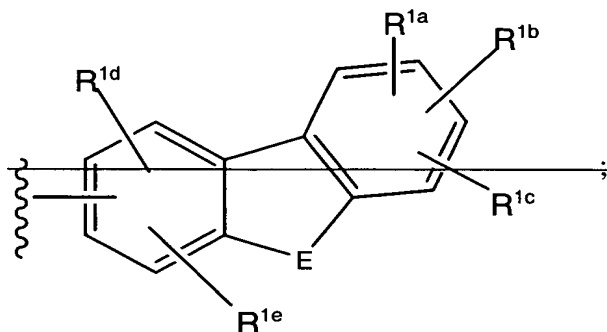
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

$-\text{NHSO}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{C}(\text{OH})\text{H}-$, $-\text{O}(\text{C}(\text{R}^9)_2)_q-$, $-\text{S}(\text{O})_m(\text{C}(\text{R}^9)_2)_q-$, $-\text{NH}(\text{C}(\text{R}^9)_2)_q-$, $-\text{NR}^{10}(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q\text{O}-$, $-(\text{C}(\text{R}^9)_2)_q\text{S}(\text{O})_m-$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}-$, $-(\text{C}(\text{R}^9)_2)_q\text{NR}^{10}-$, $-\text{C}\equiv\text{C}-$, *cis* and *trans* $-\text{CH}=\text{CH}-$ and cycloalkyl of 3 to 10 carbon atoms;

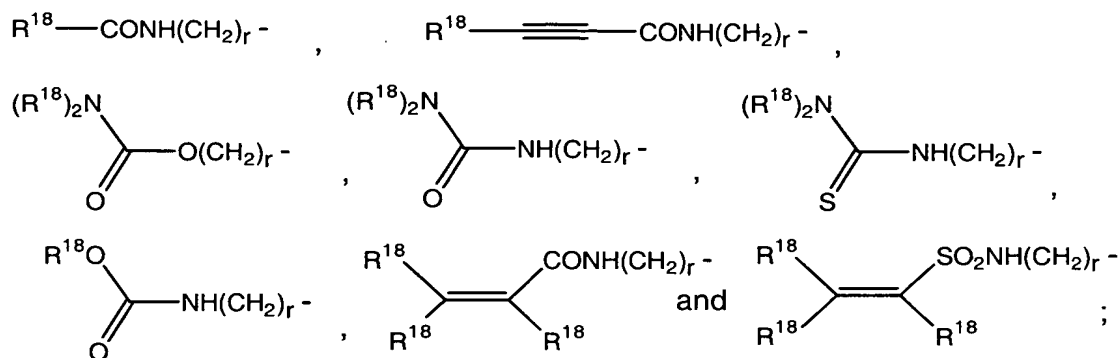
~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H, J, NO_2 , NH_2 , OH, SH, CN, N_3 , COOH , CONH_2 , $\text{NHC}(\text{O})\text{NH}_2$, $\text{C}(\text{O})\text{H}$, CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q, $\text{S}(\text{O})_m\text{R}^5$, NHSO_2R^5 , R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH , $\text{R}^6\text{S}(\text{O})_m\text{R}^5$, NHR^7OH , NHR^7OR^5 , $\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$, NHR^7NH_2 , NHR^7NHR^5 , NHR^7Q , $\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $\text{N}(\text{R}^5)\text{R}^7\text{Q}$, OR^7OH , OR^7OR^5 , OR^7NH_2 , OR^7NHR^5 , OR^7Q , $\text{OC}(\text{O})\text{R}^5$, $\text{NHC}(\text{O})\text{R}^5$, $\text{NHC}(\text{O})\text{NHR}^5$, $\text{OR}^6\text{C}(\text{O})\text{R}^5$, $\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $\text{C}(\text{O})\text{R}^5$, $\text{C}(\text{O})\text{OR}^5$, $\text{C}(\text{O})\text{NHR}^5$, $\text{C}(\text{O})\text{Q}$, $\text{R}^6\text{C}(\text{O})\text{H}$, $\text{R}^6\text{C}(\text{O})\text{R}^5$, $\text{R}^6\text{C}(\text{O})\text{OH}$, $\text{R}^6\text{C}(\text{O})\text{OR}^5$, $\text{R}^6\text{C}(\text{O})\text{NH}_2$, $\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $\text{R}^6\text{C}(\text{O})\text{Q}$, $\text{R}^6\text{OC}(\text{O})\text{R}^5$, $\text{R}^6\text{OC}(\text{O})\text{NH}_2$, $\text{R}^6\text{OC}(\text{O})\text{NHR}^5$, $\text{R}^6\text{OC}(\text{O})\text{Q}$ and YR^8 groups wherein Y is independently selected from $\text{C}(\text{O})$, $\text{C}(\text{O})\text{O}$, $\text{OC}(\text{O})$, $\text{C}(\text{O})\text{NH}$, $\text{NHC}(\text{O})$, NHSO_2 , SO_2NH , $\text{C}(\text{OH})\text{H}$, $\text{O}(\text{C}(\text{R}^9)_2)_q$, $\text{S}(\text{O})_m(\text{C}(\text{R}^9)_2)_q$, $\text{NH}(\text{C}(\text{R}^9)_2)_q$, $\text{NR}^{10}(\text{C}(\text{R}^9)_2)_q$, $(\text{C}(\text{R}^9)_2)_q$, $(\text{C}(\text{R}^9)_2)_q\text{O}$, $(\text{C}(\text{R}^9)_2)_q\text{S}(\text{O})_m$, $(\text{C}(\text{R}^9)_2)_q\text{NH}$, $(\text{C}(\text{R}^9)_2)_q\text{NR}^{10}$, $\text{C}\equiv\text{C}$, *cis* and *trans* $\text{CH}=\text{CH}$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is NH , NR^5 , O , $\text{S}(\text{O})_m$, $\text{C}(\text{O})$, CH_2 , CHR^5 or CR^5R^5 ;~~

Q is $-\text{NR}^5\text{R}^5$ and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from -H, -J, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S(O)}_m\text{R}^5$, $-\text{NH}\text{SO}_2\text{R}^5$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N(R}^5\text{)R}^7\text{OH}$, $-\text{N(R}^5\text{)R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N(R}^5\text{)R}^7\text{NH}_2$, $-\text{N(R}^5\text{)R}^7\text{NHR}^5$, $-\text{N(R}^5\text{)R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, -aryl, $-\text{CH}_2\text{aryl}$, $-\text{NHaryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{NHR}^{11}$ and $-\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from -H, -aryl, $-\text{CH}_2\text{aryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, -J, $-\text{NO}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{S(O)}_m\text{R}^5$, $-\text{NH}\text{SO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, $-\text{R}^6\text{OC(O)Q}$, $-\text{G-(C(R}^9\text{))}_p\text{-R}^{12}$, $-(\text{C(R}^9\text{)})_q\text{-R}^{12}$,~~



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S}(\text{O})_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,

$-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,

$-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,
 -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,
 -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,
 -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20
 atoms containing 1 to 4 heteroatoms which may be the same or different selected
 from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
 substituted with 1 to 4 substituents which may be the same or different selected from
 -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,
 -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,
 -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,
 -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵,
 -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH,
 -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵,
 -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H,
 -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q,
 -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}\text{R}^{17}$, $-(C(R^9)_2)_p\text{S(O)}_m\text{R}^{16}$, $-(C(R^9)_2)_p\text{CO}_2\text{R}^{16}$, $-(C(R^9)_2)_p\text{C(O)NHR}^{16}$ and

$-(C(R^9)_2)_p\text{C(O)R}^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{arylR}^{15}$, $-(C(R^9)_2)_q\text{heteroarylR}^{15}$, $-(C(R^9)_2)_q\text{heterocyclylR}^{15}$, $-(C(R^9)_2)_q\text{CO}_2\text{R}^{16}$, $-(C(R^9)_2)_q\text{C(O)NHR}^{16}$, and $-(C(R^9)_2)_q\text{C(O)R}^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_q\text{OR}^{16}$, $-(C(R^7)_2)_q\text{NR}^{16}\text{R}^{17}$, and $-(C(R^9)_2)_q\text{S(O)}_m\text{R}^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}\text{R}^{17}$, and $-(C(R^9)_2)_p\text{S(O)}_m\text{R}^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_q\text{OH}$, $-(C(R^9)_2)_q\text{OR}^{10}$, $-(C(R^9)_2)_q\text{NH}_2$, $-(C(R^9)_2)_q\text{NHR}^{10}$, $-(C(R^9)_2)_q\text{R}^{10}$, $-(C(R^9)_2)_q\text{S(O)}_m\text{R}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{R}^{10}$, $-(C(R^9)_2)_q\text{CONHR}^{10}$, $-(C(R^9)_2)_q\text{CONR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_q\text{COR}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{H}$, and $-(C(R^9)_2)_q\text{CONH}_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_p\text{OH}$, $-(C(R^9)_2)_p\text{OR}^{10}$, $-(C(R^9)_2)_p\text{NH}_2$, $-(C(R^9)_2)_p\text{NHR}^{10}$, $-(C(R^9)_2)_p\text{NR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_p\text{S(O)}_m\text{R}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{R}^{10}$, $-(C(R^9)_2)_p\text{CONHR}^{10}$, $-(C(R^9)_2)_p\text{CONR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_p\text{COR}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{H}$, and $-(C(R^9)_2)_p\text{CONH}_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6\text{NH}_2$, $-R^6\text{NHR}^5$ and $-R^6\text{Q}$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_r\text{H}$, then,

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~

b. ~~R^3 is not monosubstituted by R^{10} , $(C(R^9)_{27})_q OH$, or $(C(R^9)_{27})_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_{27})_s R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

a. ~~R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_{27}$, CO_2R^{10} ,~~

~~$CONHR^{10}$, $(C(R^9)_{27})_q OH$, $(C(R^7)_{27})_q OR^{10}$, $(C(R^9)_{27})_q NHR^{10}$, $(C(R^9)_{27})_q J$ or~~

~~$(C(R^9)_{27})_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

b. ~~R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_{27})_s R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

additionally provided that, when T and Z are carbon, then,

a. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~

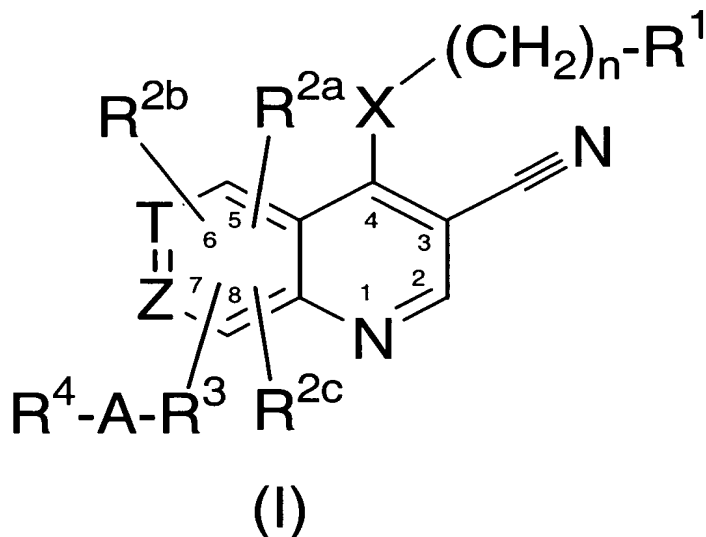
b. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

2. (original) The compound of claim 1, wherein X is $-NH-$, $-NR^5$, or $-O-$ or a pharmaceutically acceptable salt thereof.

3-4. (cancelled)

5. (re-presented – formerly claim 5) The compound of claim 1, wherein T is carbon and Z is N or a pharmaceutically acceptable salt thereof.
6. (cancelled)
7. (original) The compound of claim 1, wherein T is carbon, n is 0 and Z is N and X is –NH– or a pharmaceutically acceptable salt thereof.
- 8-9. (canceled)
10. (original) The compound of claim 1, wherein T is carbon, Z is N, X is –NH–, n is 0 and R¹ is aryl or a pharmaceutically acceptable salt thereof.
- 11-121. (canceled)
122. (currently amended) A method of treating, inhibiting the growth of , or eradicating neoplasms in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound of Formula (I) having the structure:



wherein:

X is –NH–, –NR⁵–, –O–, or –S(O)_m–;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is ~~-(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -(C(R⁹)₂)_r-C(O)-, -cycloalkyl-~~ or is absent;

T is ~~N~~ C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from ~~H, J, NO₂, NH₂, OH, SH, CN, N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁶, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(O)H, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;~~

a heteroaryl ring having 5 or 6 atoms containing 1 to 4 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected

from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

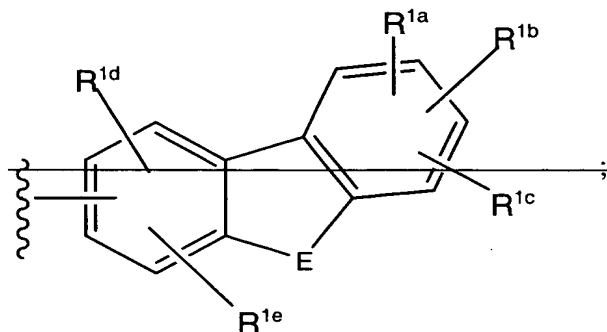
-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NH₂SO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NH₂SO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-,~~

~~$-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $C\equiv C$, *cis* and *trans* $CH=CH$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is $NH-$, NR^5- , $O-$, $S(O)_m-$, $C(O)-$, CH_2- , CHR^5- or CR^5R^5- ;~~

Q is $-NR^5R^5$ and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from H , J , NO_2 , NH_2 , OH , SH , CN , N_3 , $COOH$, $CONH_2$, $NHC(O)NH_2$, $C(O)H$, CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q , $S(O)_mR^5$, $NHSO_2R^5$, R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH ,~~

~~$R^6S(O)_mR^5$, NHR^7OH , NHR^7OR^5 , $N(R^5)R^7OH$, $N(R^5)R^7OR^5$, NHR^7NH_2 ,~~

~~NHR^7NHR^5 , NHR^7Q , $N(R^5)R^7NH_2$, $N(R^5)R^7NHR^5$, $N(R^5)R^7Q$, OR^7OH , OR^7OR^5 ,~~

~~OR^7NH_2 , OR^7NHR^5 , OR^7Q , $OC(O)R^5$, $NHC(O)R^5$, $NHC(O)NHR^5$, $OR^6C(O)R^5$,~~

~~$NHR^6C(O)R^5$, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)Q$, $R^6C(O)H$, $R^6C(O)R^5$,~~

~~$R^6C(O)OH$, $R^6C(O)OR^5$, $R^6C(O)NH_2$, $R^6C(O)NHR^5$, $R^6C(O)Q$, $R^6OC(O)R^5$,~~

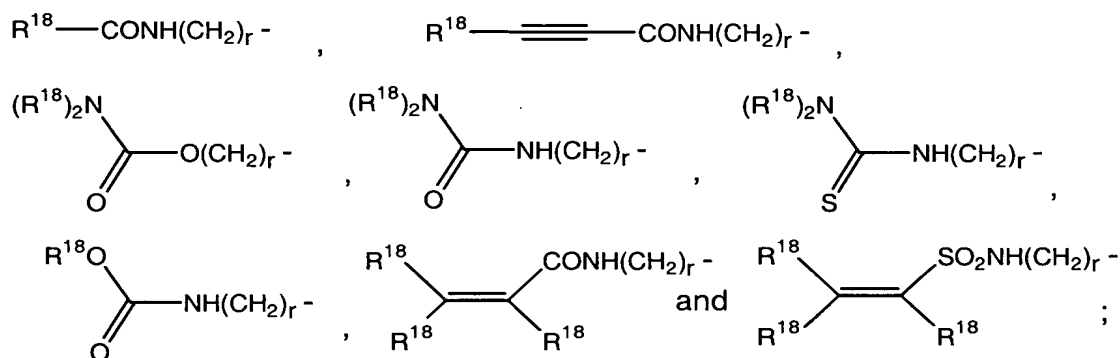
~~$R^6OC(O)NH_2$, $R^6OC(O)NHR^5$, aryl, CH_2 aryl, NH aryl, O aryl, $S(O)_m$ aryl, R^{11} ,~~

~~OR^{11} , NHR^{11} and $R^6OC(O)Q$;~~ R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from $-H$, $-aryl$, $-CH_2aryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$,

$-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6SH$, $-R^6S(O)_mR^5$, $-OR^7OH$, $-OR^7OR^5$, $-OC(O)R^5$,

$-\text{NHC(O)}\text{R}^5$, $-\text{NHC(O)}\text{NHR}^5$, $-\text{OR}^6\text{C(O)}\text{R}^5$, $-\text{NHR}^6\text{C(O)}\text{R}^5$, $-\text{C(O)}\text{R}^5$, $-\text{C(O)}\text{OR}^5$,

$-\text{C(O)}\text{NHR}^5$, $-\text{C(O)}\text{Q}$, $-\text{R}^6\text{C(O)}\text{H}$, $-\text{R}^6\text{C(O)}\text{R}^5$, $-\text{R}^6\text{C(O)}\text{OH}$, $-\text{R}^6\text{C(O)}\text{OR}^5$, $-\text{R}^6\text{C(O)}\text{NH}_2$,
 $-\text{R}^6\text{C(O)}\text{NHR}^5$, $-\text{R}^6\text{C(O)}\text{Q}$, $-\text{R}^6\text{OC(O)}\text{R}^5$, $-\text{R}^6\text{OC(O)}\text{NH}_2$, $-\text{R}^6\text{OC(O)}\text{NHR}^5$, $-\text{R}^6\text{OC(O)}\text{Q}$,
 $-\text{G}-(\text{C}(\text{R}^9)_2)_p-\text{R}^{12}$, $-(\text{C}(\text{R}^9)_2)_q-\text{R}^{12}$,



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S(O)}_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$,
 $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$;

R^4 is selected from $-(\text{C}(\text{R}^9)_2)_r\text{H}$, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$,

$-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$,

$-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$,

$-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$,
 $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring
 system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same
 or different selected from N, O and S wherein the bicyclic heteroaryl ring system may
 be optionally substituted with 1 to 4 substituents which may be the same or different
 selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$,
 $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,
 $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and
 $-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms,
 preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to
 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6
 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted
 with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms
 optionally substituted with 1 to 4 substituents which may be the same or different
 selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$,
 $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$,
 $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHCO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$,
 $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$,
 $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$,
 $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$,
 $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$,
 $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a
 heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or
 2 heteroatoms which may be the same or different, selected from N, O and S
 wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents
 which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$,
 $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-\text{C}(\text{O})\text{H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S}(\text{O})_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$,
 $-\text{NHR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S}(\text{O})_m\text{R}^5$, $-\text{NHR}^7\text{OH}$,
 $-\text{NHR}^7\text{OR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $-\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$,
 $-\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $-\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$,
 $-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{R}^6\text{R}^{12}$, $-\text{NHC}(\text{O})\text{NHR}^5$, $-\text{OR}^6\text{C}(\text{O})\text{R}^5$, $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$,
 $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$, $-\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{C}(\text{O})\text{H}$, $-\text{R}^6\text{C}(\text{O})\text{R}^5$, $-\text{R}^6\text{C}(\text{O})\text{OH}$,
 $-\text{R}^6\text{C}(\text{O})\text{OR}^5$, $-\text{R}^6\text{C}(\text{O})\text{NH}_2$, $-\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{OC}(\text{O})\text{R}^5$, $-\text{R}^6\text{OC}(\text{O})\text{NH}_2$,
 $-\text{R}^6\text{OC}(\text{O})\text{NHR}^5$ and $-\text{R}^6\text{OC}(\text{O})\text{Q}$; a bicyclic heteroaryl ring system having 8 to 20
atoms containing 1 to 4 heteroatoms which may be the same or different selected
from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
substituted with 1 to 4 substituents which may be the same or different selected from
 $-\text{H}$, $-\text{aryl}$, $-\text{CH}_2\text{aryl}$, $-\text{NHaryl}$, $-\text{Oaryl}$, $-\text{S}(\text{O})_m\text{aryl}$, $-\text{J}$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$,
 $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$,
 $-\text{S}(\text{O})_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{NHR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$,
 $-\text{R}^6\text{SH}$, $-\text{R}^6\text{R}^{12}$, $-\text{R}^6\text{S}(\text{O})_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $-\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$,
 $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $-\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{Q}$, $-\text{OR}^7\text{OH}$,
 $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{NHR}^5$,
 $-\text{OR}^6\text{C}(\text{O})\text{R}^5$, $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$, $-\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{C}(\text{O})\text{H}$,
 $-\text{R}^6\text{C}(\text{O})\text{R}^5$, $-\text{R}^6\text{C}(\text{O})\text{OH}$, $-\text{R}^6\text{C}(\text{O})\text{OR}^5$, $-\text{R}^6\text{C}(\text{O})\text{NH}_2$, $-\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{Q}$,
 $-\text{R}^6\text{OC}(\text{O})\text{R}^5$, $-\text{R}^6\text{OC}(\text{O})\text{NH}_2$, $-\text{R}^6\text{OC}(\text{O})\text{NHR}^5$ and $-\text{R}^6\text{OC}(\text{O})\text{Q}$;

R^9 is independently $-\text{H}$, $-\text{F}$ or $-\text{R}^5$;

R^{10} is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R^{11} is a cycloalkyl group of 3 to 10 carbon atoms;

R^{12} is $-N(O)_n R^{13}R^{14}$ or $-N^+(R^{10}R^{13}R^{14})J^-$;

provided that when R^{12} is $N(O)_n R^{13}R^{14}$ and n is 1, R^{13} or R^{14} are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, $-(C(R^9)_2)_pS(O)_mR^{16}$, $-(C(R^9)_2)_pCO_2R^{16}$, $-(C(R^9)_2)_pC(O)NHR^{16}$ and

$-(C(R^9)_2)_pC(O)R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_qCO_2R^{16}$, $-(C(R^9)_2)_qC(O)NHR^{16}$, and $-(C(R^9)_2)_qC(O)R^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_qOR^{16}$, $-(C(R^7)_2)_qNR^{16}R^{17}$, and $-(C(R^9)_2)_qS(O)_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, and $-(C(R^9)_2)_pS(O)_mR^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$,

$-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$,

$-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_pOH$, $-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$, $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$, $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~
- b. ~~R^3 is not monosubstituted by R^{10} , $(C(R^9)_2)_q OH$, or $(C(R^9)_2)_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_2)_6 R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

- a. ~~R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} , $CONHR^{10}$, $(C(R^9)_2)_q OH$, $(C(R^9)_2)_q OR^{10}$, $(C(R^9)_2)_q NHR^{10}$, $(C(R^9)_2)_q J$ or $(C(R^9)_2)_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- b. ~~R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_2)_6 R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

additionally provided that, when T and Z are carbon, then,

- a. ~~carbon 8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{14} when carbon 5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon 5 of Formula (I) via carbon 2 of the imidazole, oxazole or thiazole ring; and~~
- b. ~~carbon 8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{14} when X is O and carbon 5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

123. (original) The method according to claim 122 wherein the neoplasm is selected from the group consisting of breast, kidney, bladder, mouth, larynx, esophagus, stomach, colon, ovary, lung, pancreas, skin, liver, prostate and brain.

124. (original) The method of claim 122 wherein the neoplasm expresses Src or wherein the neoplasm depends at least in part on the Src pathway.

125. (original) The method of claim 122 wherein the neoplasm expresses raf or wherein the neoplasm depends at least in part on the raf pathway.

126. (original) The method of claim 122 wherein the neoplasm expresses EGFr, erbB-2, erbB-3 or erbB-4 or wherein the neoplasm depends at least in part on an EGFr, erbB-2, erbB-3 or erbB-4 pathway.

127. (original) The method of claim 122 wherein the neoplasm expresses KDR or flt-1 or wherein the neoplasm depends at least in part on a KDR or flt-1 pathway.

128. (original) The method of claim 122 wherein the neoplasm expresses PDGFr or wherein the neoplasm depends at least in part on the PDGFr pathway.

129. (original) The method of claim 122 wherein the neoplasm expresses FGFr or wherein the neoplasm depends at least in part on the FGFr pathway.

130. (original) The method of claim 122 wherein the neoplasm expresses tie-1 or tie-2 or wherein the neoplasm depends at least in part on a tie-1 or tie-2 pathway.

131. (original) The method of claim 122 wherein the neoplasm expresses EPH or wherein the neoplasm depends at least in part on the EPH pathway.

132. (original) The method of claim 122 wherein the neoplasm expresses a non-receptor tyrosine kinase including Abl, Jak, Fak, Syk or Csk or wherein the neoplasm depends at least in part on a Abl, Jak, Fak, Syk or Csk pathway.

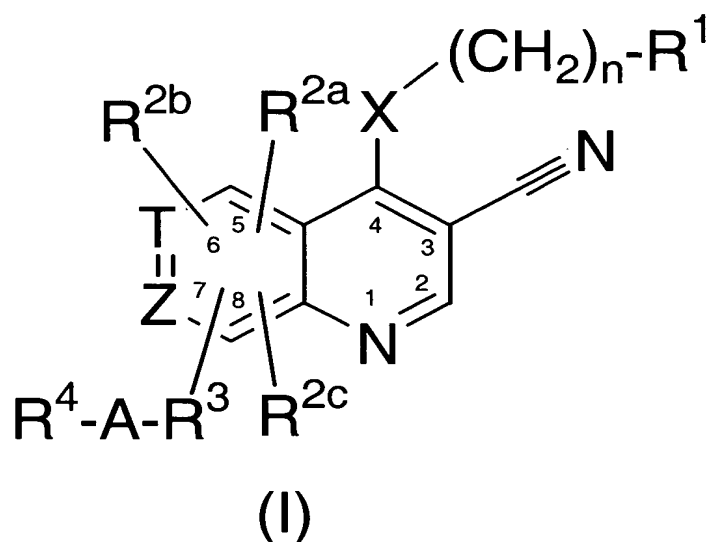
133. (original) The method of claim 122 wherein the neoplasm expresses mek or erk or wherein the neoplasm depends at least in part on the MAPK pathway.

134. (original) The method of claim 122 wherein the neoplasm expresses a cyclin dependent kinase or wherein the neoplasm depends at least in part on a cyclin dependent kinase pathway.

135. (original) The method of claim 122 wherein the neoplasm expresses a Src family kinase including Yes, Lck or Lyn or wherein the neoplasm depends at least in part on a Src family kinase pathway.

136. (original) The method of claim 122 wherein the neoplasm expresses PKA, PKB or PKC or wherein the neoplasm depends at least in part on a PKA, PKB or PKC pathway.

137. (currently amended) A method of treating, inhibiting the progression of, or eradicating polycystic kidney disease in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound of Formula (I) having the structure:



wherein:

X is -NH- , $\text{-NR}^5\text{-}$, -O- , or $\text{-S(O)}_m\text{-}$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is ~~-(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -C(R⁹)₂-, C(O)-, -cycloalkyl-~~ or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(O)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

a heteroaryl ring having 5 or 6 atoms containing 1 to ~~4~~ 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

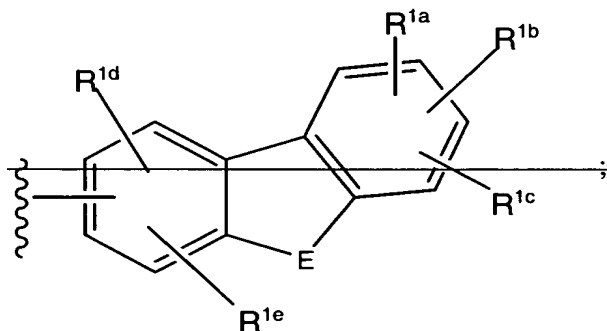
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

$-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(O)NH-$, $-NHC(O)-$,

$-NHOSO_2-$, $-SO_2NH-$, $-C(OH)H-$, $-O(C(R^9)_2)_q-$, $-S(O)_m(C(R^9)_2)_q-$, $-NH(C(R^9)_2)_q-$, $-NR^{10}(C(R^9)_2)_q-$, $-(C(R^9)_2)_q-$, $-(C(R^9)_2)_qO-$, $-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $-C\equiv C-$, *cis* and *trans* $-CH=CH-$ and cycloalkyl of 3 to 10 carbon atoms;

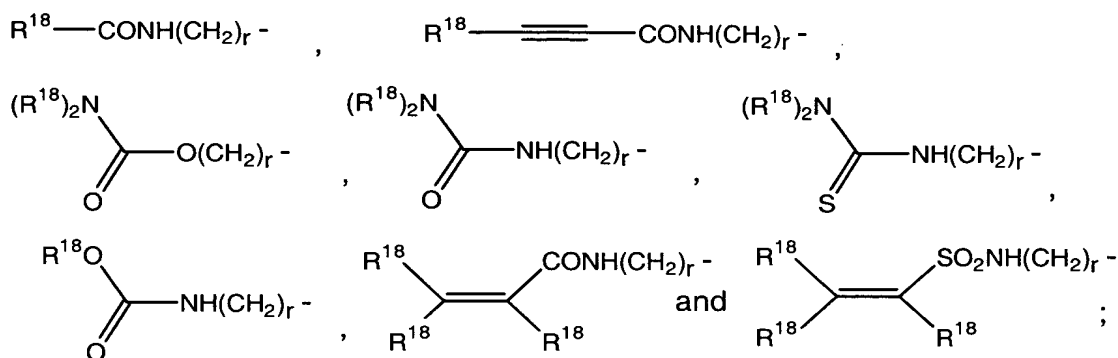
~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H , J , NO_2 , NH_2 , OH , SH , CN , N_3 , $COOH$, $CONH_2$, $NHC(O)NH_2$, $C(O)H$, CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q , $S(O)_mR^5$, $NHOSO_2R^5$, R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH , $R^6S(O)_mR^5$, NHR^7OH , NHR^7OR^5 , $N(R^5)R^7OH$, $N(R^5)R^7OR^5$, NHR^7NH_2 , NHR^7NHR^5 , NHR^7Q , $N(R^5)R^7NH_2$, $N(R^5)R^7NHR^5$, $N(R^5)R^7Q$, OR^7OH , OR^7OR^5 , OR^7NH_2 , OR^7NHR^5 , OR^7Q , $OC(O)R^5$, $NHC(O)R^5$, $NHC(O)NHR^5$, $OR^6C(O)R^5$, $NHR^6C(O)R^5$, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)Q$, $R^6C(O)H$, $R^6C(O)R^5$, $R^6C(O)OH$, $R^6C(O)OR^5$, $R^6C(O)NH_2$, $R^6C(O)NHR^5$, $R^6C(O)Q$, $R^6OC(O)R^5$, $R^6OC(O)NH_2$, $R^6OC(O)NHR^5$, $R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHOSO_2-$, $-SO_2NH-$, $-C(OH)H-$, $-O(C(R^9)_2)_q-$, $-S(O)_m(C(R^9)_2)_q-$, $-NH(C(R^9)_2)_q-$, $-NR^{10}(C(R^9)_2)_q-$, $-(C(R^9)_2)_q-$, $-(C(R^9)_2)_qO-$, $-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $-C\equiv C-$, *cis* and *trans* $-CH=CH-$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is NH , NR^5 , O , S(O)_m , C(O) , CH_2 , CHR^5 or CR^5R^5 ;~~

Q is NR^5R^5 and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from H , J , NO_2 , NH_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, NHR^7OH , NHR^7OR^5 , $\text{N(R}^5\text{)R}^7\text{OH}$, $\text{N(R}^5\text{)R}^7\text{OR}^5$, NHR^7NH_2 , NHR^7NHR^5 , NHR^7Q , $\text{N(R}^5\text{)R}^7\text{NH}_2$, $\text{N(R}^5\text{)R}^7\text{NHR}^5$, $\text{N(R}^5\text{)R}^7\text{Q}$, OR^7OH , OR^7OR^5 , OR^7NH_2 , OR^7NHR^5 , OR^7Q , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 , C(O)NHR^5 , C(O)Q , $\text{R}^6\text{C(O)H}$, $\text{R}^6\text{C(O)R}^5$, $\text{R}^6\text{C(O)OH}$, $\text{R}^6\text{C(O)OR}^5$, $\text{R}^6\text{C(O)NH}_2$, $\text{R}^6\text{C(O)NHR}^5$, $\text{R}^6\text{C(O)Q}$, $\text{R}^6\text{OC(O)R}^5$, $\text{R}^6\text{OC(O)NH}_2$, $\text{R}^6\text{OC(O)NHR}^5$, aryl , CH_2aryl , NHaryl , Oaryl , $\text{S(O)}_m\text{aryl}$, R^{11} , OR^{11} , NHR^{11} and $\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from H , aryl , CH_2aryl , Oaryl , $\text{S(O)}_m\text{aryl}$, J , NO_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^{11} , OR^{11} , R^6OH , R^6OR^5 , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, OR^7OH , OR^7OR^5 , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 , C(O)NHR^5 , C(O)Q , $\text{R}^6\text{C(O)H}$, $\text{R}^6\text{C(O)R}^5$, $\text{R}^6\text{C(O)OH}$, $\text{R}^6\text{C(O)OR}^5$, $\text{R}^6\text{C(O)NH}_2$, $\text{R}^6\text{C(O)NHR}^5$, $\text{R}^6\text{C(O)Q}$, $\text{R}^6\text{OC(O)R}^5$, $\text{R}^6\text{OC(O)NH}_2$, $\text{R}^6\text{OC(O)NHR}^5$, $\text{R}^6\text{OC(O)Q}$, $\text{G-(C(R}^9\text{))}_p\text{-R}^{12}$, $\text{-(C(R}^9\text{))}_q\text{-R}^{12}$,~~



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S}(\text{O})_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,

$-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,

$-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,
 -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,
 -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,
 -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20
 atoms containing 1 to 4 heteroatoms which may be the same or different selected
 from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
 substituted with 1 to 4 substituents which may be the same or different selected from
 -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,
 -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,
 -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,
 -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵,
 -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH,
 -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵,
 -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H,
 -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q,
 -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R^{13} and R^{14} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, $-(C(R^9)_2)_pS(O)_mR^{16}$, $-(C(R^9)_2)_pCO_2R^{16}$, $-(C(R^9)_2)_pC(O)NHR^{16}$ and

$-(C(R^9)_2)_pC(O)R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_qCO_2R^{16}$, $-(C(R^9)_2)_qC(O)NHR^{16}$, and $-(C(R^9)_2)_qC(O)R^{15}$; or optionally substituted on carbon by $-F$, $-(C(R^7)_2)_qOR^{16}$, $-(C(R^7)_2)_qNR^{16}R^{17}$, and $-(C(R^9)_2)_qS(O)_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, and $-(C(R^9)_2)_pS(O)_mR^{16}$;

R^{15} is independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$, $-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_pOH$, $-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$, $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$, $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of $-H$, $-\text{aryl}$, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,

- a. R^2 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or

~~b. R^3 is not monosubstituted by R^{10} , $(C(R^9)_{27})_q OH$, or $(C(R^9)_{27})_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

~~c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_{27})_6 R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

~~a. R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} ,~~

~~$CONHR^{10}$, $(C(R^9)_{27})_q OH$, $(C(R^7)_{27})_q OR^{10}$, $(C(R^9)_{27})_q NHR^{10}$, $(C(R^9)_{27})_q J$ or~~

~~$(C(R^9)_{27})_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

~~b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_{27})_6 R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

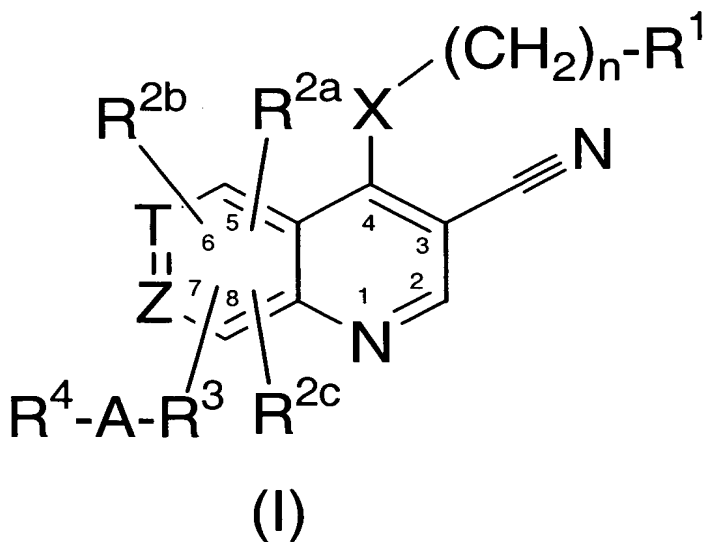
additionally provided that, when T and Z are carbon, then,

~~a. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~

~~b. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

138. (Currently Amended) A method of treating, inhibiting the progression of, or eradicating polycystic kidney disease in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound of Formula (I) having the structure:



wherein:

X is -NH- , $\text{-NR}^5\text{-}$, -O- , or $\text{-S(O)}_m\text{-}$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is $\text{-(C(R}^9\text{)}_2\text{)}_r\text{-}$, -C(O)- , $\text{-C(O)(C(R}^9\text{)}_2\text{)}_r\text{-}$, $\text{-(C(R}^9\text{)}_2\text{)}_r\text{C(O)-}$, -cycloalkyl- or is absent;

T is N and Z is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of

~~6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;~~

a heteroaryl ring having 5 or 6 atoms containing 1 to ~~4~~ 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

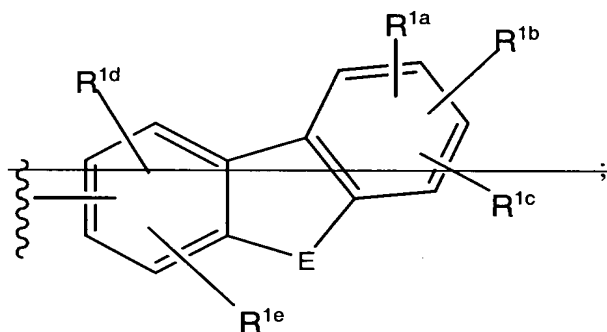
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, (C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

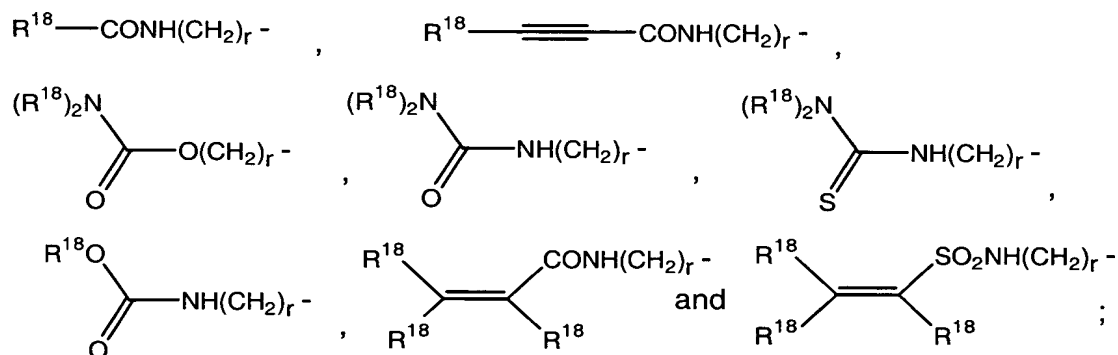
a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵, NHR⁵, Q, S(O)_mR⁵, NHSO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH, R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂, NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵, OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵, NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵, R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵, R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from C(O), C(O)O, OC(O), C(O)NH, NHC(O), NHSO₂, SO₂NH, C(OH)H, O(C(R⁹)₂)_q, S(O)_m(C(R⁹)₂)_q, NH(C(R⁹)₂)_q, NR¹⁰(C(R⁹)₂)_q, (C(R⁹)₂)_q, (C(R⁹)₂)_qO, (C(R⁹)₂)_qS(O)_m, (C(R⁹)₂)_qNH, (C(R⁹)₂)_qNR¹⁰, C≡C, *cis* and *trans* CH=CH and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula



E is NH, NR⁵, O, S(O)_m, C(O), CH₂, CHR⁵ or CR⁵R⁵;

Q is -NR⁵R⁵ and further provided that when each R⁵ is independently selected from alkyl and alkenyl, R⁵R⁵ may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~$R^{1a}, R^{1b}, R^{1c}, R^{1d}$ and R^{1e} are each, independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -R¹¹, -OR¹¹, -NHR¹¹ and -R⁶OC(O)Q; R^{2a}, R^{2b} , and R^{2c} , are each, independently selected from -H, -aryl, -CH₂aryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶SH, -R⁶S(O)_mR⁵, -OR⁷OH, -OR⁷OR⁵, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q, -G-(C(R⁹)₂)_p-R¹², -(C(R⁹)₂)_q-R¹²,~~



G is -NH-, -NR¹⁰-, -O- or -S(O)_m-;

R³ is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂,

-CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,

-(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and

-G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹²,

-CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰,

-(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH;

R⁴ is selected from -(C(R⁹)₂)_rH, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰,

-CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R⁸ is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -R⁶R¹², -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵,

-C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂,

-C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹,

-NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH,

-NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q,

-N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,

-C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,

-R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,

-R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,

-R⁶SH, -, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R¹³ and R¹⁴ are independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl-R¹⁵, -(C(R⁹)₂)_qheteroaryl-R¹⁵, -(C(R⁹)₂)_qheterocyclyl-R¹⁵, -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, -(C(R⁹)₂)_pS(O)_mR¹⁶, -(C(R⁹)₂)_pCO₂R¹⁶, -(C(R⁹)₂)_pC(O)NHR¹⁶ and

-(C(R⁹)₂)_pC(O)R¹⁵; further provided that R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, -R⁵, -R¹¹, -(C(R⁹)₂)_qarylR¹⁵, -(C(R⁹)₂)_qheteroarylR¹⁵, -(C(R⁹)₂)_qheterocyclylR¹⁵, -(C(R⁹)₂)_qCO₂R¹⁶, -(C(R⁹)₂)_qC(O)NHR¹⁶, and -(C(R⁹)₂)_qC(O)R¹⁵; or optionally substituted on carbon by -F, -(C(R⁷)₂)_qOR¹⁶, -(C(R⁷)₂)_qNR¹⁶R¹⁷, and -(C(R⁹)₂)_qS(O)_mR¹⁶; or optionally substituted on nitrogen by -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, and -(C(R⁹)₂)_pS(O)_mR¹⁶;

R^{15} is independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_q\text{OH}$, $-(C(R^9)_2)_q\text{OR}^{10}$, $-(C(R^9)_2)_q\text{NH}_2$, $-(C(R^9)_2)_q\text{NHR}^{10}$, $-(C(R^9)_2)_q\text{R}^{10}$, $-(C(R^9)_2)_q\text{S(O)}_m\text{R}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{R}^{10}$, $-(C(R^9)_2)_q\text{CONHR}^{10}$, $-(C(R^9)_2)_q\text{CONR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_q\text{COR}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{H}$, and $-(C(R^9)_2)_q\text{CONH}_2$;

R^{16} and R^{17} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_p\text{OH}$, $-(C(R^9)_2)_p\text{OR}^{10}$, $-(C(R^9)_2)_p\text{NH}_2$, $-(C(R^9)_2)_p\text{NHR}^{10}$, $-(C(R^9)_2)_p\text{NR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_p\text{S(O)}_m\text{R}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{R}^{10}$, $-(C(R^9)_2)_p\text{CONHR}^{10}$, $-(C(R^9)_2)_p\text{CONR}^{10}\text{R}^{10}$, $-(C(R^9)_2)_p\text{COR}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{H}$, and $-(C(R^9)_2)_p\text{CONH}_2$;

R^{18} is independently selected from the group consisting of $-H$, $-\text{aryl}$, $-R^5$, $-R^6\text{NH}_2$, $-R^6\text{NHR}^5$ and $-R^6\text{Q}$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_r\text{H}$, then,

- a. R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or
- b. R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_2)_q\text{OH}$, or $-(C(R^9)_2)_q\text{OR}^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and
- c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_2)_6\text{R}^{12}$ and R^{12} is $\text{NR}^{13}\text{R}^{14}$;

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

- a. R^4 is not substituted by $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-(C(R^9)_2)_q\text{OH}$, $-(C(R^9)_2)_q\text{OR}^{10}$, $-(C(R^9)_2)_q\text{NHR}^{10}$, $-(C(R^9)_2)_q\text{J}$ or $-(C(R^9)_2)_q\text{NH}_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and

b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^8)_2)_s R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;

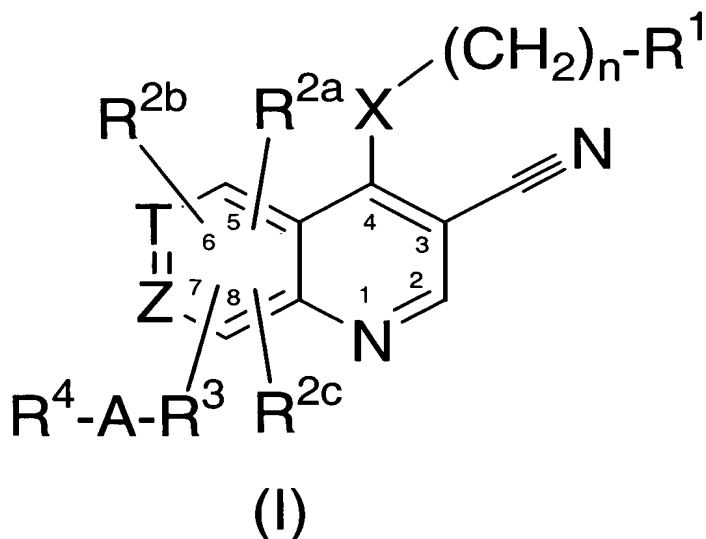
additionally provided that, when T and Z are carbon, then,

a. carbon-8 is not substituted by $-OH$, $-OR^{10}$, $-SR^{10}$, or $-OR^{11}$ when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and

b. carbon-8 is not substituted by $-OH$, $-OR^{10}$, $-SR^{10}$, or $-OR^{11}$ when X is $-O-$ and carbon-5 is substituted by aryl or heteroaryl;

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

139. (Currently Amended) A method of treating a disease or inhibiting a disease state whose etiology is at least in part caused by a defect in a signaling pathway upstream from a protein kinase; by overexpression of a protein kinase; or by a dysregulated protein kinase in a mammal in need thereof which comprises providing said mammal an effective amount of a compound of Formula (I),



wherein:

X is -NH- , $\text{-NR}^5\text{-}$, -O- , or $\text{-S(O)}_m\text{-}$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is $\text{-(C(R}^9)_2)_r\text{-}$, -C(O)- , $\text{-C(O)(C(R}^9)_2)_r\text{-}$, $\text{-(C(R}^9)_2)_r\text{C(O)-}$, -cycloalkyl- or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

~~R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁶, OR⁶, NHR⁶, Q, S(O)_mR⁶, NHSO₂R⁶, R⁶OH, R⁶OR⁶, R⁶NH₂, R⁶NHR⁶, R⁶Q, R⁶SH, R⁶S(O)_mR⁶, NHR⁷OH, NHR⁷OR⁶, N(R⁶)R⁷OH, N(R⁶)R⁷OR⁶, NHR⁷NH₂, NHR⁷NHR⁶, NHR⁷Q, N(R⁶)R⁷NH₂, N(R⁶)R⁷NHR⁶, N(R⁶)R⁷Q, OR⁷OH, OR⁷OR⁶, OR⁷NH₂, OR⁷NHR⁶, OR⁷Q, OC(O)R⁶, NHC(O)R⁶, NHC(O)NHR⁶, OR⁶C(O)R⁶, NHR⁶C(O)R⁶, C(O)R⁶, C(O)OR⁶, C(O)NHR⁶, C(O)Q, R⁶C(O)H, R⁶C(O)R⁶, R⁶C(O)OH, R⁶C(O)OR⁶,~~

~~R⁶C(O)NH₂, R⁶C(O)NHR⁶, R⁶C(O)Q, R⁶OC(O)R⁶, R⁶OC(O)NH₂, R⁶OC(O)NHR⁶, R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from C(O), C(O)O, OC(O), C(O)NH, NHC(O), NHSO₂, SO₂NH, C(OH)H, O(C(R⁹)₂)_q, S(O)_m(C(R⁹)₂)_q, NH(C(R⁹)₂)_q, NR¹⁰(C(R⁹)₂)_q, (C(R⁹)₂)_q, (C(R⁹)₂)_qO,~~

~~-(C(R⁹)₂)_qS(O)_m, -(C(R⁹)₂)_qNH, -(C(R⁹)₂)_qNR¹⁰, -C≡C-, *cis* and *trans*-CH=CH- and cycloalkyl of 3 to 10 carbon atoms;~~

a heteroaryl ring having ~~5 or 6~~ atoms containing 1 to ~~4~~ 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

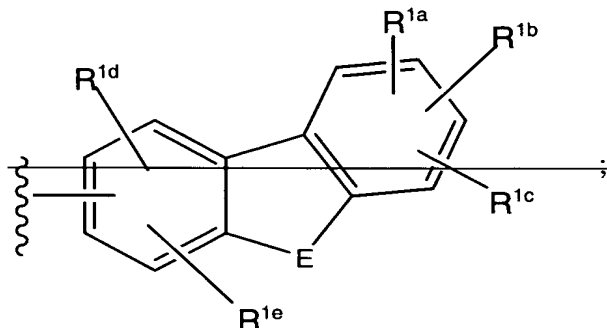
-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NH₂SO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans*-CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵,~~

~~$-R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHSO_2-$, $-SO_2NH-$, $-C(OH)H-$, $-O(C(R^9)_2)_q-$, $-S(O)_m(C(R^9)_2)_q-$, $-NH(C(R^9)_2)_q-$, $-NR^{10}(C(R^9)_2)_q-$, $-(C(R^9)_2)_q-$, $-(C(R^9)_2)_qO-$, $-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $-C\equiv C-$, *cis* and *trans* $-CH=CH-$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is $-NH-$, $-NR^5-$, $-O-$, $-S(O)_m-$, $-C(O)-$, $-CH_2-$, $-CHR^5-$ or $-CR^5R^5-$;~~

Q is $-NR^5R^5$ and further provided that when each R⁵ is independently selected from alkyl and alkenyl, R⁵R⁵ may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

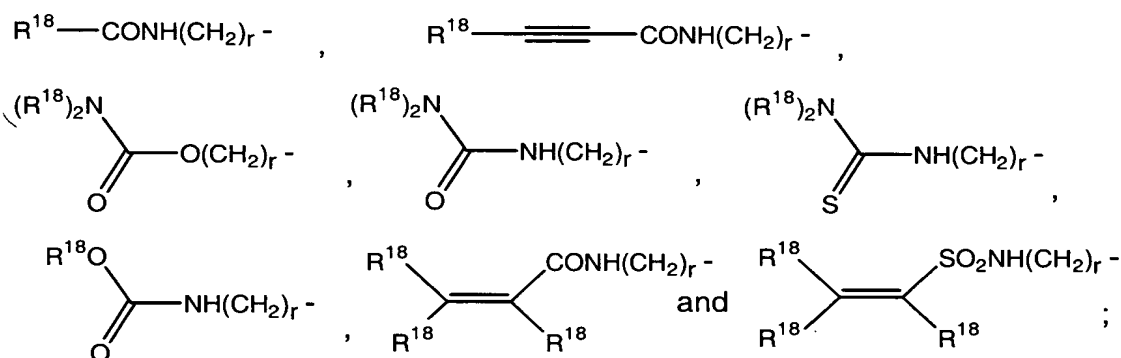
~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from H, J, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, aryl, $-CH_2$ aryl, $-NH$ aryl, $-O$ aryl, $-S(O)_m$ aryl, $-R^{1+}$,~~

$-\text{OR}^{11}$, $-\text{NHR}^{11}$ and $-\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from $-\text{H}$, $-\text{aryl}$, $-\text{CH}_2\text{aryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, $-\text{J}$, $-\text{NO}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$,

$-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{S(O)}_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OC(O)R}^5$,

$-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$,

$-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, $-\text{R}^6\text{OC(O)Q}$, $-\text{G}-(\text{C(R}^9)_2)_p-\text{R}^{12}$, $-(\text{C(R}^9)_2)_q-\text{R}^{12}$,



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S(O)}_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C(R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C(R}^9)_2)_q\text{OH}$, $-(\text{C(R}^9)_2)_q\text{OR}^{10}$, $-(\text{C(R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C(R}^9)_2)_q\text{J}$, $-(\text{C(R}^9)_2)_q\text{NH}_2$, $-(\text{C(R}^9)_2)_r\text{H}$, $-\text{G}(\text{C(R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C(R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C(R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C(R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C(R}^9)_2)_q\text{OH}$, $-(\text{C(R}^9)_2)_q\text{OR}^{10}$, $-(\text{C(R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C(R}^9)_2)_q\text{J}$, $-(\text{C(R}^9)_2)_q\text{NH}_2$, $-(\text{C(R}^9)_2)_r\text{H}$, $-\text{G}(\text{C(R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C(R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C(R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C(R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C(R}^9)_2)_q\text{OH}$, $-(\text{C(R}^9)_2)_q\text{OR}^{10}$, $-(\text{C(R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C(R}^9)_2)_q\text{J}$, $-(\text{C(R}^9)_2)_q\text{NH}_2$, $-(\text{C(R}^9)_2)_r\text{H}$, $-\text{G}(\text{C(R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C(R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C(R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be

optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$,

$-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{H}$, $-\text{aryl}$, $-\text{CH}_2\text{aryl}$, $-\text{NHaryl}$, $-\text{Oaryl}$, $-\text{S}(\text{O})_m\text{aryl}$, $-\text{J}$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S}(\text{O})_m\text{R}^5$, $-\text{NH}\text{SO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{NHR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S}(\text{O})_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $-\text{R}^6\text{R}^{12}$, $-\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $-\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{NHR}^5$, $-\text{OR}^6\text{C}(\text{O})\text{R}^5$, $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$,

-C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂,

-C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹,

-NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH,

-NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q,

-N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,

-C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,

-R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,

-R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,

-R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R^{10} is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R^{11} is a cycloalkyl group of 3 to 10 carbon atoms;

R^{12} is $-N(O)_n R^{13}R^{14}$ or $-N^+(R^{10}R^{13}R^{14})J^-$;

provided that when R^{12} is $N(O)_n R^{13}R^{14}$ and n is 1, R^{13} or R^{14} are not H;

R^{13} and R^{14} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, $-(C(R^9)_2)_pS(O)_mR^{16}$, $-(C(R^9)_2)_pCO_2R^{16}$, $-(C(R^9)_2)_pC(O)NHR^{16}$ and

$-(C(R^9)_2)_pC(O)R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_qCO_2R^{16}$, $-(C(R^9)_2)_qC(O)NHR^{16}$, and $-(C(R^9)_2)_qC(O)R^{15}$; or optionally substituted on carbon by $-F$, $-(C(R^7)_2)_qOR^{16}$, $-(C(R^7)_2)_qNR^{16}R^{17}$, and $-(C(R^9)_2)_qS(O)_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, and $-(C(R^9)_2)_pS(O)_mR^{16}$;

R^{15} is independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$, $-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_pOH$,

$-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$,
 $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$,
 $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, ~~the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,~~

- ~~a. R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~
- ~~b. R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_2)_qOH$, or $-(C(R^9)_2)_qOR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- ~~c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_2)_6R^{12}$ and R^{12} is $-NR^{13}R^{14}$;~~

~~further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,~~

- ~~a. R^4 is not substituted by $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$ or $-(C(R^9)_2)_qNH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- ~~b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^9)_2)_6R^{12}$ and s is 0 and R^{12} is $-NR^{13}R^{14}$;~~

~~additionally provided that, when T and Z are carbon, then,~~

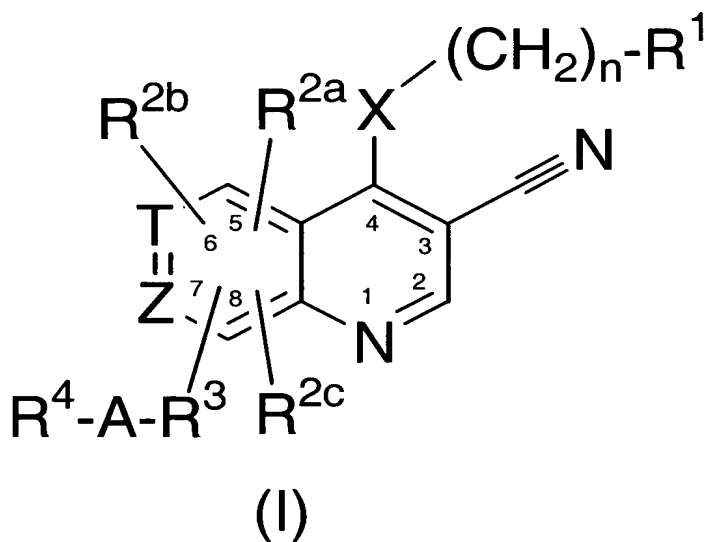
- ~~a. carbon 8 is not substituted by $-OH$, $-OR^{10}$, $-SR^{10}$, or $-OR^{14}$ when carbon 5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein~~

~~the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~

~~b. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

~~further provided that when either T or Z are N, then R^{2c} is absent; or a pharmaceutically acceptable salt thereof.~~

140. (Currently Amended) A method of inhibiting the biological effects of a deregulated protein kinase in a mammal which comprises administering to said mammal an effective amount of a compound of Formula (I),



wherein:

X is -NH- , $\text{-NR}^5\text{-}$, -O- , or $\text{-S(O)}_m\text{-}$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is ~~-(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -(C(R⁹)₂)_rC(O)-, -cycloalkyl-~~ or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

a heteroaryl ring having 5 or 6 atoms containing 1 to 4 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

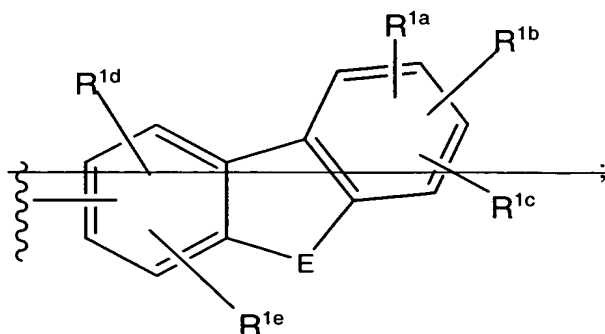
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NH₂SO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵, NHR⁵, Q, S(O)_mR⁵, NH₂SO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH, R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂, NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵, OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵, NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵, R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵, R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from C(O), C(O)O, OC(O), C(O)NH, NHC(O), NH₂SO₂, SO₂NH, C(OH)H, O(C(R⁹)₂)_q-, S(O)_m(C(R⁹)₂)_q-, NH(C(R⁹)₂)_q-, NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, (C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~

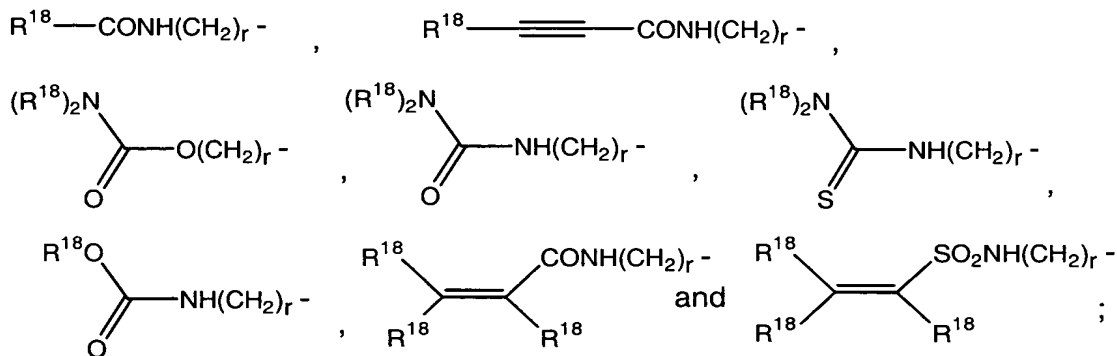


E is NH , NR^5 , O , S(O)_m , C(O) , CH_2 , CHR^5 or CR^5R^5 ;

Q is NR^5R^5 and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from H , J , NO_2 , NH_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, NHR^7OH , NHR^7OR^5 , $\text{N(R}^5\text{)R}^7\text{OH}$, $\text{N(R}^5\text{)R}^7\text{OR}^5$, NHR^7NH_2 , NHR^7NHR^5 , NHR^7Q , $\text{N(R}^5\text{)R}^7\text{NH}_2$, $\text{N(R}^5\text{)R}^7\text{NHR}^5$, $\text{N(R}^5\text{)R}^7Q$, OR^7OH , OR^7OR^5 , OR^7NH_2 , OR^7NHR^5 , OR^7Q , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 , C(O)NHR^5 , C(O)Q , $\text{R}^6\text{C(O)H}$, $\text{R}^6\text{C(O)R}^5$, $\text{R}^6\text{C(O)OH}$, $\text{R}^6\text{C(O)OR}^5$, $\text{R}^6\text{C(O)NH}_2$, $\text{R}^6\text{C(O)NHR}^5$, $\text{R}^6\text{C(O)Q}$, $\text{R}^6\text{OC(O)R}^5$, $\text{R}^6\text{OC(O)NH}_2$, $\text{R}^6\text{OC(O)NHR}^5$, aryl , CH_2aryl , NHaryl , Oaryl , $\text{S(O)}_m\text{aryl}$, R^{14} , OR^{14} , NHR^{14} and $\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from H , aryl , CH_2aryl , Oaryl , $\text{S(O)}_m\text{aryl}$, J , NO_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^{11} , OR^{11} , R^6OH , R^6OR^5 , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, OR^7OH , OR^7OR^5 , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 ,

-C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂,
 -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q,
 -G-(C(R⁹)₂)_p-R¹², -(C(R⁹)₂)_q-R¹²,



G is -NH-, -NR¹⁰-, -O- or -S(O)_m-;

R³ is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,

-(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and

-G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein

the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$,
 $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$,
 $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$,
 $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$,
 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$,
 $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$,
 $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$,
 $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring

system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NH SO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NH SO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,
 $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,
 $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,
 $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-R^6R^{12}$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$,
 $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$,
 $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$,
 $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a bicyclic heteroaryl ring system having 8 to 20
atoms containing 1 to 4 heteroatoms which may be the same or different selected
from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
substituted with 1 to 4 substituents which may be the same or different selected from
-H, -aryl, $-CH_2$ aryl, -NHaryl, -Oaryl, $-S(O)_m$ aryl, -J, $-NO_2$, $-NH_2$, -OH, -SH, -CN, $-N_3$,
 $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, -Q,
 $-S(O)_mR^5$, $-NH SO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$,
 $-R^6SH$, $-R^6R^{12}$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$,
 $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$,
 $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$,
 $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$,
 $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$,
 $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$;

R^9 is independently -H, -F or $-R^5$;

R^{10} is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R^{11} is a cycloalkyl group of 3 to 10 carbon atoms;

R^{12} is $-N(O)_n R^{13}R^{14}$ or $-N^+(R^{10}R^{13}R^{14})J^-$;

provided that when R^{12} is $N(O)_n R^{13}R^{14}$ and n is 1, R^{13} or R^{14} are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, $-(C(R^9)_2)_pS(O)_mR^{16}$, $-(C(R^9)_2)_pCO_2R^{16}$, $-(C(R^9)_2)_pC(O)NHR^{16}$ and

$-(C(R^9)_2)_pC(O)R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_qCO_2R^{16}$, $-(C(R^9)_2)_qC(O)NHR^{16}$, and $-(C(R^9)_2)_qC(O)R^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_qOR^{16}$, $-(C(R^7)_2)_qNR^{16}R^{17}$, and $-(C(R^9)_2)_qS(O)_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, and $-(C(R^9)_2)_pS(O)_mR^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$, $-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_pOH$, $-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$, $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$, $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, the 6-position is substituted when ~~T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,~~

a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~

b. ~~R^3 is not monosubstituted by R^{10} , $(C(R^9)_{27})_q OH$, or $(C(R^9)_{27})_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_{27})_6 R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

a. ~~R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} ,~~

~~$CONHR^{10}$, $(C(R^9)_{27})_q OH$, $(C(R^9)_{27})_q OR^{10}$, $(C(R^9)_{27})_q NHR^{10}$, $(C(R^9)_{27})_q J$ or~~

~~$(C(R^9)_{27})_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

b. ~~R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_{27})_6 R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

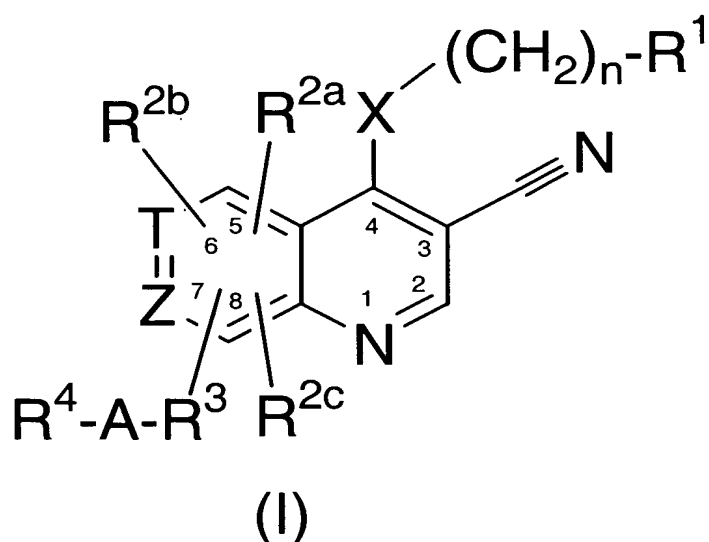
additionally provided that, when T and Z are carbon, then,

a. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~

b. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

141. (Currently Amended) A pharmaceutical composition for treating or inhibiting disease in a mammal characterized by abnormal growth of cells which comprises administering to a mammal in need thereof an effective amount of a compound of Formula (I) having the structure:



wherein:

X is $-\text{NH}-$, $-\text{NR}^5-$, $-\text{O}-$, or $-\text{S}(\text{O})_m-$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is $-(\text{C}(\text{R}^9)_2)_r-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})(\text{C}(\text{R}^9)_2)_r-$, $-(\text{C}(\text{R}^9)_2)_r\text{C}(\text{O})-$, $-\text{cycloalkyl}-$ or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

~~R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(O)H, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, (C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C=C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;~~

a heteroaryl ring having 5 or 6 atoms containing 1 to 4 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

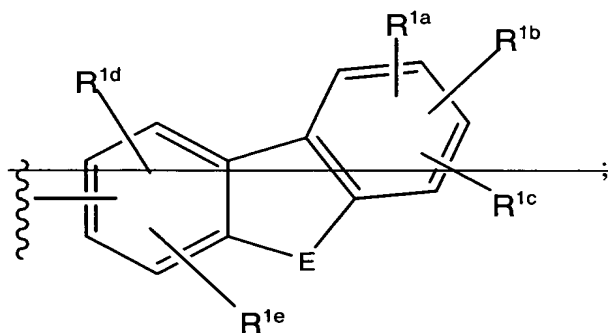
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

~~-NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-,
-NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-,
-(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon
atoms;~~

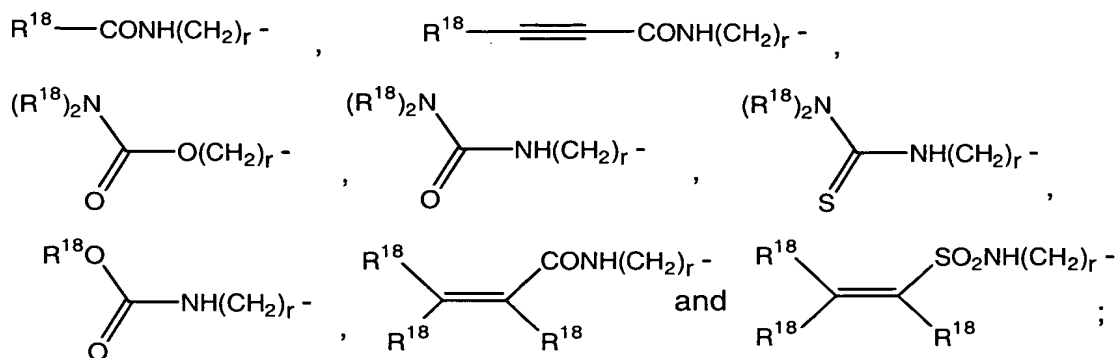
~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms
which may be the same or different selected from N, O and S wherein the bicyclic
heteroaryl ring system may be optionally substituted with 1 to 4 substituents which
may be the same or different selected from H, J, NO₂, NH₂, OH, SH, CN, N₃,
-COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,
-S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵,
-NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q,
-N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵,
-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵,
-C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵,
-R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵,
-R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-,
-C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-,
-S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-,
(C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and
cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is -NH-, -NR⁵-, -O-, -S(O)_m-, -C(O)-, -CH₂-, -CHR⁵- or -CR⁵R⁵-;~~

Q is $-\text{NR}^5\text{R}^5$ and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from -H, -J, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S(O)}_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N(R}^5\text{)R}^7\text{OH}$, $-\text{N(R}^5\text{)R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N(R}^5\text{)R}^7\text{NH}_2$, $-\text{N(R}^5\text{)R}^7\text{NHR}^5$, $-\text{N(R}^5\text{)R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, -aryl, $-\text{CH}_2\text{aryl}$, $-\text{NHaryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, R^{11} , $-\text{OR}^{11}$, $-\text{NHR}^{11}$ and $-\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from -H, -aryl, $-\text{CH}_2\text{aryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, -J, $-\text{NO}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{S(O)}_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, $-\text{R}^6\text{OC(O)Q}$, $-\text{G-(C(R}^9\text{))}_p\text{-R}^{12}$, $-(\text{C(R}^9\text{)})_q\text{-R}^{12}$,~~



G is -NH-, -NR¹⁰-, -O- or -S(O)_m-;

R³ is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and

-G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹²,

-CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and
 $-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,

$-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,

$-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,
 -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,
 -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,
 -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20
 atoms containing 1 to 4 heteroatoms which may be the same or different selected
 from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
 substituted with 1 to 4 substituents which may be the same or different selected from
 -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,
 -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,
 -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,
 -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵,
 -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH,
 -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵,
 -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H,
 -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q,
 -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}R^{17}$, $-(C(R^9)_2)_p\text{S(O)}_mR^{16}$, $-(C(R^9)_2)_p\text{CO}_2R^{16}$, $-(C(R^9)_2)_p\text{C(O)NHR}^{16}$ and

$-(C(R^9)_2)_p\text{C(O)R}^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicycyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_q\text{CO}_2R^{16}$, $-(C(R^9)_2)_q\text{C(O)NHR}^{16}$, and $-(C(R^9)_2)_p\text{C(O)R}^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_q\text{OR}^{16}$, $-(C(R^7)_2)_q\text{NR}^{16}R^{17}$, and $-(C(R^9)_2)_q\text{S(O)}_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}R^{17}$, and $-(C(R^9)_2)_p\text{S(O)}_mR^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_q\text{OH}$, $-(C(R^9)_2)_q\text{OR}^{10}$, $-(C(R^9)_2)_q\text{NH}_2$, $-(C(R^9)_2)_q\text{NHR}^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_q\text{S(O)}_mR^{10}$, $-(C(R^9)_2)_q\text{CO}_2R^{10}$, $-(C(R^9)_2)_q\text{CONHR}^{10}$, $-(C(R^9)_2)_q\text{CONR}^{10}R^{10}$, $-(C(R^9)_2)_q\text{COR}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{H}$, and $-(C(R^9)_2)_q\text{CONH}_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_p\text{OH}$, $-(C(R^9)_2)_p\text{OR}^{10}$, $-(C(R^9)_2)_p\text{NH}_2$, $-(C(R^9)_2)_p\text{NHR}^{10}$, $-(C(R^9)_2)_p\text{NR}^{10}R^{10}$, $-(C(R^9)_2)_p\text{S(O)}_mR^{10}$, $-(C(R^9)_2)_p\text{CO}_2R^{10}$, $-(C(R^9)_2)_p\text{CONHR}^{10}$, $-(C(R^9)_2)_p\text{CONR}^{10}R^{10}$, $-(C(R^9)_2)_p\text{COR}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{H}$, and $-(C(R^9)_2)_p\text{CONH}_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6\text{NH}_2$, $-R^6\text{NHR}^5$ and $-R^6\text{Q}$;

provided that, the 6-position is substituted when ~~T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_r\text{H}$, then,~~

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~

~~b. R^3 is not monosubstituted by R^{10} , $(C(R^9)_2)_q OH$, or $(C(R^9)_2)_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

~~c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_2)_6 R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

~~further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,~~

~~a. R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} ,~~

~~$CONHR^{10}$, $(C(R^9)_2)_q OH$, $(C(R^9)_2)_q OR^{10}$, $(C(R^9)_2)_q NHR^{10}$, $(C(R^9)_2)_q J$ or~~

~~$(C(R^9)_2)_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

~~b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_2)_6 R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

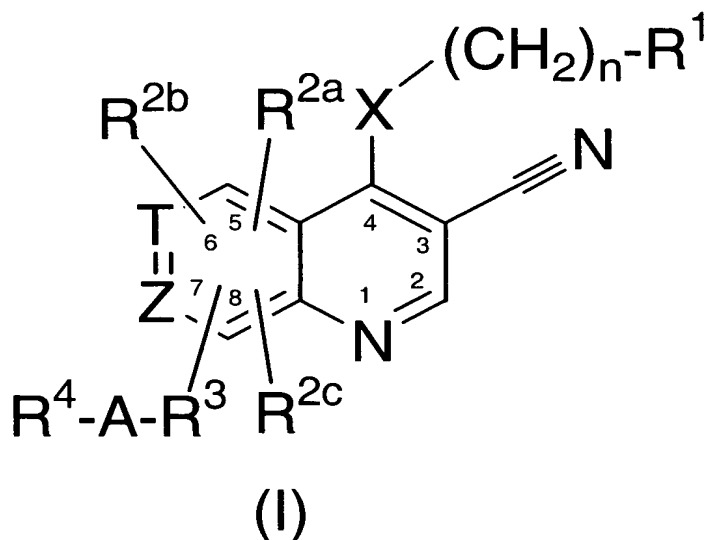
~~additionally provided that, when T and Z are carbon, then,~~

~~a. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~

~~b. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

~~further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.~~

142. (Currently Amended) A method of treating or inhibiting the progression of restenosis in a mammal in need thereof which comprises providing to said mammal an effective amount of a PDGFr kinase inhibitor of Formula (I), having the structure



wherein:

X is -NH-, -NR⁵-, -O-, or -S(O)_m-;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is ~~-(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -(C(R⁹)₂)_r-C(O)-, -cycloalkyl-~~ or is absent;

T is ~~N~~ C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(O)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C=C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

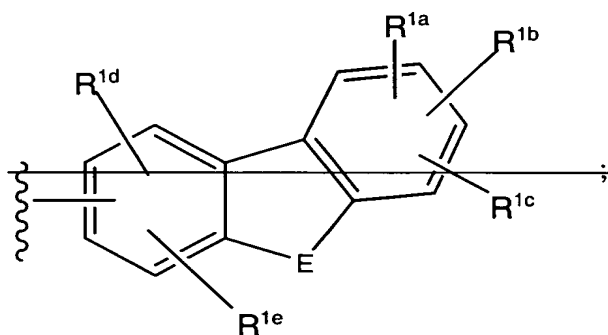
a heteroaryl ring having 5 or 6 atoms containing 1 to 4 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

$-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(O)NH-$, $-NHC(O)-$,

$-NHOSO_2-$, $-SO_2NH-$, $-C(OH)H-$, $-O(C(R^9)_2)_q-$, $-S(O)_m(C(R^9)_2)_q-$, $-NH(C(R^9)_2)_q-$, $-NR^{10}(C(R^9)_2)_q-$, $-(C(R^9)_2)_q-$, $-(C(R^9)_2)_qO-$, $-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $-C\equiv C-$, *cis* and *trans* $-CH=CH-$ and cycloalkyl of 3 to 10 carbon atoms;

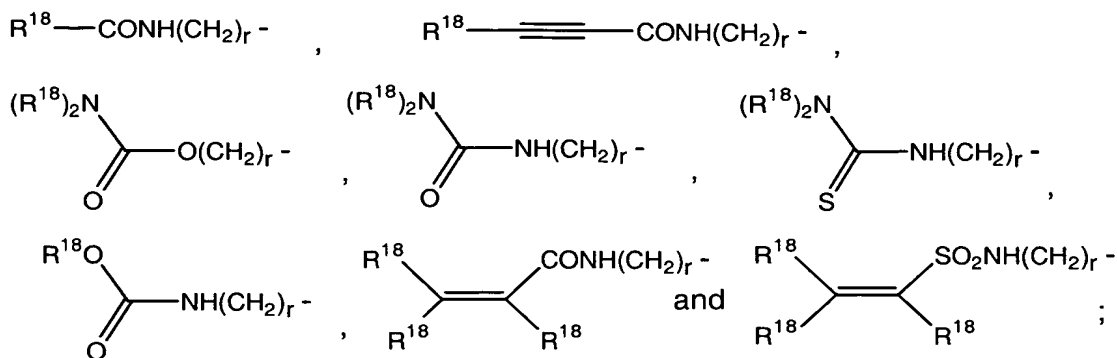
~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H, J, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from $-C(O)-$, $-C(O)O-$, $-OC(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHOSO_2-$, $-SO_2NH-$, $-C(OH)H-$, $-O(C(R^9)_2)_q-$, $-S(O)_m(C(R^9)_2)_q-$, $-NH(C(R^9)_2)_q-$, $-NR^{10}(C(R^9)_2)_q-$, $-(C(R^9)_2)_q-$, $-(C(R^9)_2)_qO-$, $-(C(R^9)_2)_qS(O)_m-$, $-(C(R^9)_2)_qNH-$, $-(C(R^9)_2)_qNR^{10}-$, $-C\equiv C-$, *cis* and *trans* $-CH=CH-$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



E is ~~NH, NR⁵, O, S(O)_m, C(O), CH₂, CHR⁵ or CR⁵R⁵~~;

Q is -NR⁵R⁵ and further provided that when each R⁵ is independently selected from alkyl and alkenyl, R⁵R⁵ may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a}, R^{1b}, R^{1c}, R^{1d} and R^{1e} are each, independently selected from H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵, NHR⁵, Q, S(O)_mR⁵, NHSO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH, R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂, NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵, OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵, NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵, R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵, R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, aryl, CH₂aryl, NHaryl, Oaryl, S(O)_maryl, R¹¹, OR¹¹, NHR¹¹ and R⁶OC(O)Q; R^{2a}, R^{2b}, and R^{2c}, are each, independently selected from -H, -aryl, -CH₂aryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶SH, -R⁶S(O)_mR⁵, -OR⁷OH, -OR⁷OR⁵, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q, -G-(C(R⁹)₂)_p-R¹², -(C(R⁹)₂)_q-R¹²,~~



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S}(\text{O})_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{OH}$, $-(\text{C}(\text{R}^9)_2)_q\text{OR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{NHR}^{10}$, $-(\text{C}(\text{R}^9)_2)_q\text{J}$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}_2$, $-(\text{C}(\text{R}^9)_2)_r\text{H}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OR}^{10}$, $-\text{G}(\text{C}(\text{R}^9)_2)_p\text{R}^{12}$, and

$-\text{G}(\text{C}(\text{R}^9)_2)_p\text{OH}$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{R}^{10}$, $-(\text{C}(\text{R}^9)_2)_s\text{R}^{12}$,

$-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$, $-\text{CO}_2\text{R}^{10}$, $-\text{CONHR}^{10}$, $-\text{COR}^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and
 $-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$,

$-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$,

$-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,

$-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,

$-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,
 -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,
 -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,
 -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20
 atoms containing 1 to 4 heteroatoms which may be the same or different selected
 from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
 substituted with 1 to 4 substituents which may be the same or different selected from
 -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,
 -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,
 -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,
 -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵,
 -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH,
 -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵,
 -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H,
 -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q,
 -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}R^{17}$, $-(C(R^9)_2)_p\text{S(O)}_mR^{16}$, $-(C(R^9)_2)_p\text{CO}_2R^{16}$, $-(C(R^9)_2)_p\text{C(O)NHR}^{16}$ and

$-(C(R^9)_2)_p\text{C(O)}R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_q\text{CO}_2R^{16}$, $-(C(R^9)_2)_q\text{C(O)NHR}^{16}$, and $-(C(R^9)_2)_p\text{C(O)}R^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_q\text{OR}^{16}$, $-(C(R^7)_2)_q\text{NR}^{16}R^{17}$, and $-(C(R^9)_2)_q\text{S(O)}_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_p\text{OR}^{16}$, $-(C(R^9)_2)_p\text{NR}^{16}R^{17}$, and $-(C(R^9)_2)_p\text{S(O)}_mR^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_q\text{OH}$, $-(C(R^9)_2)_q\text{OR}^{10}$, $-(C(R^9)_2)_q\text{NH}_2$, $-(C(R^9)_2)_q\text{NHR}^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_q\text{S(O)}_mR^{10}$, $-(C(R^9)_2)_q\text{CO}_2R^{10}$, $-(C(R^9)_2)_q\text{CONHR}^{10}$, $-(C(R^9)_2)_q\text{CONR}^{10}R^{10}$, $-(C(R^9)_2)_q\text{COR}^{10}$, $-(C(R^9)_2)_q\text{CO}_2\text{H}$, and $-(C(R^9)_2)_q\text{CONH}_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_p\text{OH}$, $-(C(R^9)_2)_p\text{OR}^{10}$, $-(C(R^9)_2)_p\text{NH}_2$, $-(C(R^9)_2)_p\text{NHR}^{10}$, $-(C(R^9)_2)_p\text{NR}^{10}R^{10}$, $-(C(R^9)_2)_p\text{S(O)}_mR^{10}$, $-(C(R^9)_2)_p\text{CO}_2R^{10}$, $-(C(R^9)_2)_p\text{CONHR}^{10}$, $-(C(R^9)_2)_p\text{CONR}^{10}R^{10}$, $-(C(R^9)_2)_p\text{COR}^{10}$, $-(C(R^9)_2)_p\text{CO}_2\text{H}$, and $-(C(R^9)_2)_p\text{CONH}_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6\text{NH}_2$, $-R^6\text{NHR}^5$ and $-R^6\text{Q}$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_r\text{H}$, then,

- a. R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or

b. R^3 is not monosubstituted by R^{10} , $(C(R^9)_{27})_q OH$, or $(C(R^9)_{27})_q OR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and

c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $(C(R^9)_{27})_6 R^{12}$ and R^{12} is $NR^{13}R^{14}$;

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

a. R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_{27}$, CO_2R^{10} ,

$CONHR^{10}$, $(C(R^9)_{27})_q OH$, $(C(R^7)_{27})_q OR^{10}$, $(C(R^9)_{27})_q NHR^{10}$, $(C(R^9)_{27})_q J$ or

$(C(R^9)_{27})_q NH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and

b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $(C(R^9)_{27})_6 R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;

additionally provided that, when T and Z are carbon, then,

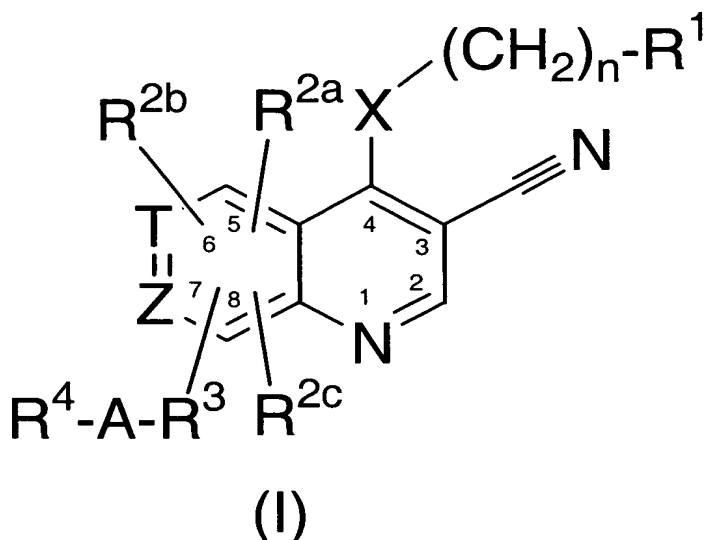
a. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and

b. carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

143. (Currently Amended) A method of treating, inhibiting or eradicating autoimmune diseases which include rheumatoid arthritis, sepsis and transplant rejection in a mammal in need thereof which comprises providing to said

mammal an effective amount of a Zap-70 or Lck kinase inhibitor of Formula (I),
having the structure:



wherein:

X is -NH- , $\text{-NR}^5\text{-}$, -O- , or $\text{-S(O)}_m\text{-}$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is $\text{-(C(R}^9\text{)}_2\text{)}_r\text{-}$, -C(O)- , $\text{-C(O)(C(R}^9\text{)}_2\text{)}_r\text{-}$, $\text{-(C(R}^9\text{)}_2\text{)C(O)-}$, -cycloalkyl- or is absent;

T is N, C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of

6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from ~~H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵, NHR⁵, Q, S(O)_mR⁵, NHSO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH, R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂, NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵, OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵, NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵, R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵, R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from C(O)-, C(O)O-, OC(O)-, C(O)NH-, NHC(O)-, NHSO₂-, SO₂NH-, C(OH)H-, O(C(R⁹)₂)_q-, S(O)_m(C(R⁹)₂)_q-, NH(C(R⁹)₂)_q-, NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, (C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;~~

a heteroaryl ring having 5 or 6 atoms containing 1 to ~~4~~ 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

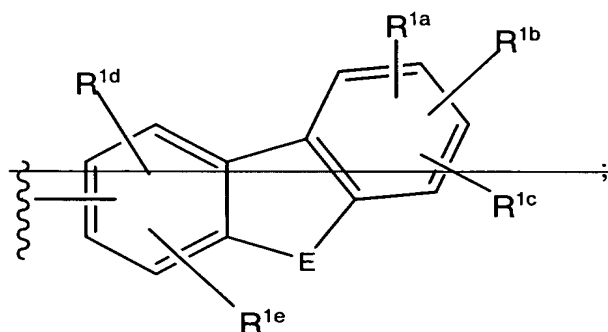
-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

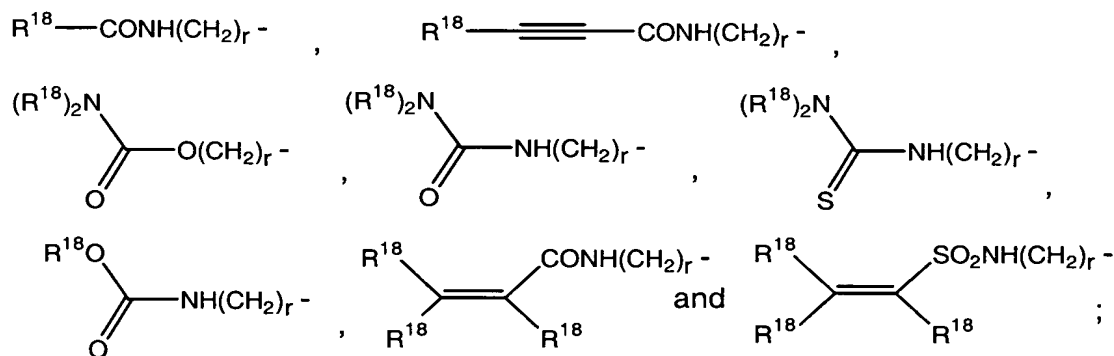
a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from H, J, NO₂, NH₂, OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵, NHR⁵, Q, S(O)_mR⁵, NHSO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH, R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂, NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵, OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵, NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵, R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵, R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from C(O), C(O)O, OC(O), C(O)NH, NHC(O), NHSO₂, SO₂NH, C(OH)H, O(C(R⁹)₂)_q, S(O)_m(C(R⁹)₂)_q, NH(C(R⁹)₂)_q, NR¹⁰(C(R⁹)₂)_q, (C(R⁹)₂)_q, (C(R⁹)₂)_qO, (C(R⁹)₂)_qS(O)_m, (C(R⁹)₂)_qNH, (C(R⁹)₂)_qNR¹⁰, C≡C, *cis* and *trans* CH=CH and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula



E is ~~NH, NR⁵, O, S(O)_m, C(O), CH₂, CHR⁵ or CR⁵R⁵~~;

Q is ~~NR⁵R⁵~~ and further provided that when each R⁵ is independently selected from alkyl and alkenyl, R⁵R⁵ may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from $-H$, $-J$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S(O)}_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N(R}^5\text{)R}^7\text{OH}$, $-\text{N(R}^5\text{)R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N(R}^5\text{)R}^7\text{NH}_2$, $-\text{N(R}^5\text{)R}^7\text{NHR}^5$, $-\text{N(R}^5\text{)R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, $-\text{aryl}$, $-\text{CH}_2\text{aryl}$, $-\text{NHaryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, $-\text{R}^{14}$, $-\text{OR}^{14}$, $-\text{NHR}^{14}$ and $-\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from $-H$, $-\text{aryl}$, $-\text{CH}_2\text{aryl}$, $-\text{Oaryl}$, $-\text{S(O)}_m\text{aryl}$, $-J$, $-\text{NO}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC(O)NH}_2$, $-\text{C(O)H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{S(O)}_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^{11}$, $-\text{OR}^{11}$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S(O)}_m\text{R}^5$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OC(O)R}^5$, $-\text{NHC(O)R}^5$, $-\text{NHC(O)NHR}^5$, $-\text{OR}^6\text{C(O)R}^5$, $-\text{NHR}^6\text{C(O)R}^5$, $-\text{C(O)R}^5$, $-\text{C(O)OR}^5$, $-\text{C(O)NHR}^5$, $-\text{C(O)Q}$, $-\text{R}^6\text{C(O)H}$, $-\text{R}^6\text{C(O)R}^5$, $-\text{R}^6\text{C(O)OH}$, $-\text{R}^6\text{C(O)OR}^5$, $-\text{R}^6\text{C(O)NH}_2$, $-\text{R}^6\text{C(O)NHR}^5$, $-\text{R}^6\text{C(O)Q}$, $-\text{R}^6\text{OC(O)R}^5$, $-\text{R}^6\text{OC(O)NH}_2$, $-\text{R}^6\text{OC(O)NHR}^5$, $-\text{R}^6\text{OC(O)Q}$, $-\text{G}-(\text{C(R}^9)_2)_p\text{-R}^{12}$, $-(\text{C(R}^9)_2)_q\text{-R}^{12}$,



G is $-\text{NH}-$, $-\text{NR}^{10}-$, $-\text{O}-$ or $-\text{S(O)}_m-$;

R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-\text{R}^{10}$, $-(\text{C(R}^9)_2)_s\text{R}^{12}$, $-\text{CHO}$, 1,3-dioxolane, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$, $-\text{CONH}_2$.

-CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,

-(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and

-G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹²,

-CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰,

-(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH;

R⁴ is selected from -(C(R⁹)₂)_rH, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰,

-CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -R⁶R¹², -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵,

-C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂,

-C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹,

-NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH,

-NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q,

-N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵,

-OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵,

-C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH,

-R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂,

-R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,

-R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_nR¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_nR¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R¹³ and R¹⁴ are independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl-R¹⁵, -(C(R⁹)₂)_qheteroaryl-R¹⁵, -(C(R⁹)₂)_qheterocyclyl-R¹⁵, -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, -(C(R⁹)₂)_pS(O)_mR¹⁶, -(C(R⁹)₂)_pCO₂R¹⁶, -(C(R⁹)₂)_pC(O)NHR¹⁶ and

-(C(R⁹)₂)_pC(O)R¹⁵; further provided that R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, -R⁵, -R¹¹, -(C(R⁹)₂)_qarylR¹⁵, -(C(R⁹)₂)_qheteroarylR¹⁵, -(C(R⁹)₂)_qheterocyclylR¹⁵, -(C(R⁹)₂)_qCO₂R¹⁶, -(C(R⁹)₂)_qC(O)NHR¹⁶, and -(C(R⁹)₂)_qC(O)R¹⁵; or optionally substituted on carbon by -F, -(C(R⁷)₂)_qOR¹⁶, -(C(R⁷)₂)_qNR¹⁶R¹⁷, and -(C(R⁹)₂)_qS(O)_mR¹⁶; or optionally substituted on nitrogen by -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, and -(C(R⁹)₂)_pS(O)_mR¹⁶;

R^{15} is independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q$ aryl, $-(C(R^9)_2)_q$ heteroaryl, $-(C(R^9)_2)_q$ heterocyclyl, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$, $-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of $-H$, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q$ aryl, $-(C(R^9)_2)_q$ heteroaryl, $-(C(R^9)_2)_q$ heterocyclyl, $-(C(R^9)_2)_pOH$, $-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$, $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$, $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of $-H$, $-aryl$, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~
- b. ~~R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_2)_qOH$, or $-(C(R^9)_2)_qOR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_2)_6R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

- a. ~~R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} , $CONHR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$ or $-(C(R^9)_2)_qNH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~

b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^9)_2)_6R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;

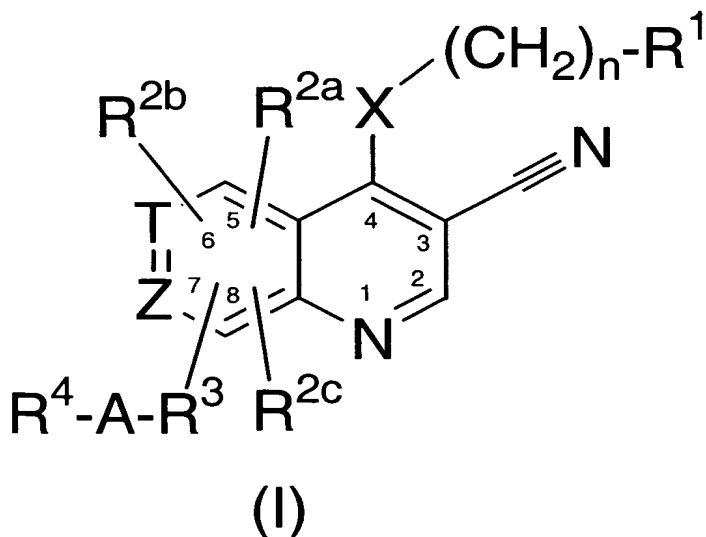
additionally provided that, when T and Z are carbon, then,

a. carbon 8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon 5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon 5 of Formula (I) via carbon 2 of the imidazole, oxazole or thiazole ring; and

b. carbon 8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon 5 is substituted by aryl or heteroaryl;

further provided that when either T or Z are N, then R^{2c} is absent; or a pharmaceutically acceptable salt thereof.

144. (Currently Amended) A method of treating, inhibiting or eradicating viral infections in a mammal in need thereof which comprises providing to said mammal an effective amount of a UL-97 kinase inhibitor of Formula (I), having the structure



wherein:

X is $-\text{NH}-$, $-\text{NR}^5-$, $-\text{O}-$, or $-\text{S}(\text{O})_m-$;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is $-(\text{C}(\text{R}^9)_2)_r-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})(\text{C}(\text{R}^9)_2)_r-$, $-(\text{C}(\text{R}^9)_2)_r\text{C}(\text{O})-$, $-\text{cycloalkyl}-$ or is absent;

T is N and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R^1 is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from $-\text{H}$, $-\text{J}$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$, $-\text{S}(\text{O})_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S}(\text{O})_m\text{R}^5$, $-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $-\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$, $-\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $-\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{NHR}^5$, $-\text{OR}^6\text{C}(\text{O})\text{R}^5$, $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$, $-\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{C}(\text{O})\text{H}$, $-\text{R}^6\text{C}(\text{O})\text{R}^5$, $-\text{R}^6\text{C}(\text{O})\text{OH}$, $-\text{R}^6\text{C}(\text{O})\text{OR}^5$, $-\text{R}^6\text{C}(\text{O})\text{NH}_2$, $-\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{OC}(\text{O})\text{R}^5$, $-\text{R}^6\text{OC}(\text{O})\text{NH}_2$, $-\text{R}^6\text{OC}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{OC}(\text{O})\text{Q}$ and $-\text{YR}^8$ groups wherein Y is independently selected from $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{OC}(\text{O})-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{NHC}(\text{O})-$, $-\text{NHSO}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{C}(\text{OH})\text{H}-$, $-\text{O}(\text{C}(\text{R}^9)_2)_q-$, $-\text{S}(\text{O})_m(\text{C}(\text{R}^9)_2)_q-$, $-\text{NH}(\text{C}(\text{R}^9)_2)_q-$, $-\text{NR}^{10}(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q\text{O}-$, $-(\text{C}(\text{R}^9)_2)_q\text{S}(\text{O})_m-$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}-$, $-(\text{C}(\text{R}^9)_2)_q\text{NR}^{10}-$, $-\text{C}\equiv\text{C}-$, *cis* and *trans* $-\text{CH}=\text{CH}-$ and cycloalkyl of 3 to 10 carbon atoms;

a heteroaryl ring having ~~5 or~~ 6 atoms containing 1 to ~~4~~ 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

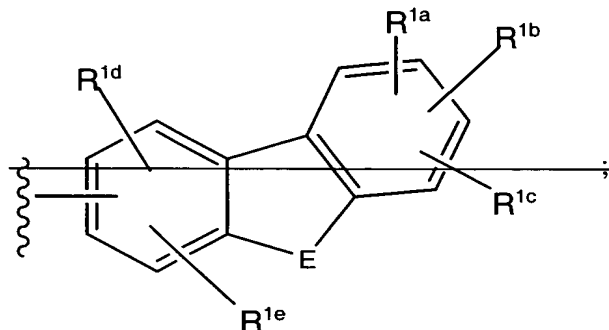
-OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -R⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵,

-R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-,

-NH₂SO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

~~a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-,~~

~~C(O)O, OC(O), C(O)NH, NHC(O), NHSO₂, SO₂NH, C(O)H, O(C(R⁹)₂)_q,
 S(O)_m(C(R⁹)₂)_q, NH(C(R⁹)₂)_q, NR¹⁰(C(R⁹)₂)_q, (C(R⁹)₂)_q, (C(R⁹)₂)_qO,
 (C(R⁹)₂)_qS(O)_m, (C(R⁹)₂)_qNH, (C(R⁹)₂)_qNR¹⁰, C=C, *cis* and *trans* CH=CH and
 cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula~~



~~E is NH, NR⁵, O, S(O)_m, C(O), CH₂, CHR⁵ or CR⁵R⁵;~~

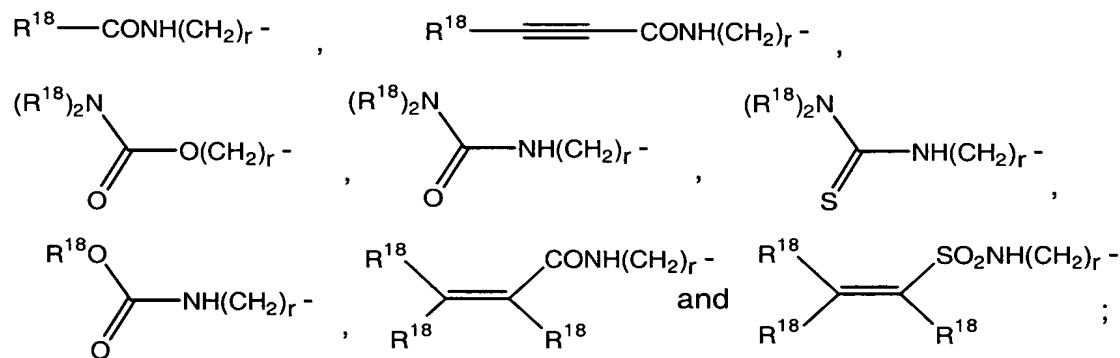
Q is ~~NR⁵R⁵~~ and further provided that when each R⁵ is independently selected from alkyl and alkenyl, R⁵R⁵ may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a}, R^{1b}, R^{1c}, R^{1d} and R^{1e} are each, independently selected from H, J, NO₂, NH₂,
 OH, SH, CN, N₃, COOH, CONH₂, NHC(O)NH₂, C(O)H, CF₃, OCF₃, R⁵, OR⁵,
 NHR⁵, Q, S(O)_mR⁵, NHSO₂R⁵, R⁶OH, R⁶OR⁵, R⁶NH₂, R⁶NHR⁵, R⁶Q, R⁶SH,
 R⁶S(O)_mR⁵, NHR⁷OH, NHR⁷OR⁵, N(R⁵)R⁷OH, N(R⁵)R⁷OR⁵, NHR⁷NH₂,
 NHR⁷NHR⁵, NHR⁷Q, N(R⁵)R⁷NH₂, N(R⁵)R⁷NHR⁵, N(R⁵)R⁷Q, OR⁷OH, OR⁷OR⁵,
 OR⁷NH₂, OR⁷NHR⁵, OR⁷Q, OC(O)R⁵, NHC(O)R⁵, NHC(O)NHR⁵, OR⁶C(O)R⁵,
 NHR⁶C(O)R⁵, C(O)R⁵, C(O)OR⁵, C(O)NHR⁵, C(O)Q, R⁶C(O)H, R⁶C(O)R⁵,
 R⁶C(O)OH, R⁶C(O)OR⁵, R⁶C(O)NH₂, R⁶C(O)NHR⁵, R⁶C(O)Q, R⁶OC(O)R⁵,
 R⁶OC(O)NH₂, R⁶OC(O)NHR⁵, aryl, CH₂aryl, NHaryl, Oaryl, S(O)_maryl, R¹¹,
 OR¹¹, NHR¹¹ and R⁶OC(O)Q; R^{2a}, R^{2b}, and R^{2c}, are each, independently selected
 from -H, -aryl, -CH₂aryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -OH, -SH, -CN, -N₃, -COOH,~~

-CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶SH, -R⁶S(O)_mR⁵, -OR⁷OH, -OR⁷OR⁵, -OC(O)R⁵,

-NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵,

-C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q, -G-(C(R⁹)₂)_p-R¹², -(C(R⁹)₂)_q-R¹²,



G is -NH-, -NR¹⁰-, -O- or -S(O)_m-;

R³ is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

-CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰,
 -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH,
 -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring
 system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same
 or different selected from N, O and S wherein the bicyclic heteroaryl ring system may
 be optionally substituted with 1 to 4 substituents which may be the same or different
 selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂,
 -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,
 -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and
 -G(C(R⁹)₂)_pOH;

R⁵ is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms,
 preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to
 6 carbon atoms;

R⁶ is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6
 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R⁷ is a divalent alkyl group of 2 to 6 carbon atoms;

R⁸ is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted
 with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms
 optionally substituted with 1 to 4 substituents which may be the same or different
 selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH,
 -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵,
 -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂,
 -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -R⁶R¹²,
 -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵,
 -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵,
 -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵,

-C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵,
 -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a
 heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or
 2 heteroatoms which may be the same or different, selected from N, O and S
 wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents

which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -R⁶R¹², -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NH₂SO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵ and -R⁶OC(O)Q;

R⁹ is independently -H, -F or -R⁵;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

R¹² is -N(O)_n R¹³R¹⁴ or -N⁺(R¹⁰R¹³R¹⁴)J⁻;

provided that when R¹² is N(O)_n R¹³R¹⁴ and n is 1, R¹³ or R¹⁴ are not H;

R¹³ and R¹⁴ are independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl-R¹⁵, -(C(R⁹)₂)_qheteroaryl-R¹⁵, -(C(R⁹)₂)_qheterocyclyl-R¹⁵, -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, -(C(R⁹)₂)_pS(O)_mR¹⁶, -(C(R⁹)₂)_pCO₂R¹⁶, -(C(R⁹)₂)_pC(O)NHR¹⁶ and

-(C(R⁹)₂)_pC(O)R¹⁵; further provided that R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, -R⁵, -R¹¹, -(C(R⁹)₂)_qarylR¹⁵, -(C(R⁹)₂)_qheteroarylR¹⁵, -(C(R⁹)₂)_qheterocyclylR¹⁵, -(C(R⁹)₂)_qCO₂R¹⁶, -(C(R⁹)₂)_qC(O)NHR¹⁶, and -(C(R⁹)₂)_qC(O)R¹⁵; or optionally substituted on carbon by -F, -(C(R⁷)₂)_qOR¹⁶, -(C(R⁷)₂)_qNR¹⁶R¹⁷, and -(C(R⁹)₂)_qS(O)_mR¹⁶; or optionally substituted on nitrogen by -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, and -(C(R⁹)₂)_pS(O)_mR¹⁶;

R¹⁵ is independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl, -(C(R⁹)₂)_qheteroaryl, -(C(R⁹)₂)_qheterocyclyl, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qR¹⁰, -(C(R⁹)₂)_qS(O)_mR¹⁰, -(C(R⁹)₂)_qCO₂R¹⁰, -(C(R⁹)₂)_qCONHR¹⁰, -(C(R⁹)₂)_qCONR¹⁰R¹⁰, -(C(R⁹)₂)_qCOR¹⁰, -(C(R⁹)₂)_qCO₂H, and -(C(R⁹)₂)_qCONH₂;

R¹⁶ and R¹⁷ are independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl, -(C(R⁹)₂)_qheteroaryl, -(C(R⁹)₂)_qheterocyclyl, -(C(R⁹)₂)_pOH, -(C(R⁹)₂)_pOR¹⁰, -(C(R⁹)₂)_pNH₂, -(C(R⁹)₂)_pNHR¹⁰, -(C(R⁹)₂)_pNR¹⁰R¹⁰, -(C(R⁹)₂)_pS(O)_mR¹⁰, -(C(R⁹)₂)_pCO₂R¹⁰, -(C(R⁹)₂)_pCONHR¹⁰, -(C(R⁹)₂)_pCONR¹⁰R¹⁰, -(C(R⁹)₂)_pCOR¹⁰, -(C(R⁹)₂)_pCO₂H, and -(C(R⁹)₂)_pCONH₂;

R¹⁸ is independently selected from the group consisting of -H, -aryl, -R⁵, -R⁶NH₂, -R⁶NHR⁵ and -R⁶Q;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_{27})_qH$, then,

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~
- b. ~~R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_{27})_qOH$, or $-(C(R^9)_{27})_qOR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_{27})_sR^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

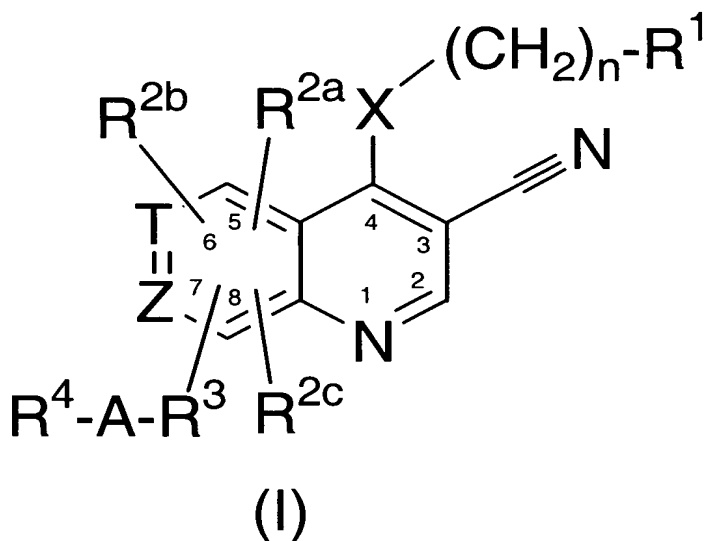
- a. ~~R^4 is not substituted by $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-(C(R^9)_{27})_qOH$, $-(C(R^9)_{27})_qOR^{10}$, $-(C(R^9)_{27})_qNHR^{10}$, $-(C(R^9)_{27})_qJ$ or $-(C(R^9)_{27})_qNH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- b. ~~R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^9)_{27})_sR^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

additionally provided that, when T and Z are carbon, then,

- a. ~~carbon-8 is not substituted by $-OH$, $-OR^{10}$, $-SR^{10}$, or $-OR^{11}$ when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~
- b. ~~carbon-8 is not substituted by $-OH$, $-OR^{10}$, $-SR^{10}$, or $-OR^{11}$ when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

145. (Currently Amended) A method of treating or inhibiting the progression of osteoporosis in a mammal in need thereof which comprises providing to said mammal an effective amount of a Src kinase inhibitor of Formula (I), having the structure



wherein:

X is -NH-, -NR⁵-, -O-, or -S(O)_m-;

n is an integer of 0 or 1;

m is an integer of 0 to 2;

q is an integer of 0 to 5;

p is an integer of 2 to 5;

s is an integer of 0 to 5;

r is an integer of 0 to 5;

J is halogen;

A is ~~-(C(R⁹)₂)_r-, -C(O)-, -C(O)(C(R⁹)₂)_r-, -(C(R⁹)₂)_r-C(O)-, -cycloalkyl-~~ or is absent;

T is N C and Z are each independently is carbon N, provided that both T and Z are not simultaneously N;

R¹ is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, (C(R⁹)₂)_q-, (C(R⁹)₂)_qO-, -C(R⁹)₂)_qS(O)_m-, (C(R⁹)₂)_qNH-, (C(R⁹)₂)_qNR¹⁰-, C≡C-, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂,

-OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -R⁷OR⁵,

$-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$, $-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{R}^5$,
 $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$, $-\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{C}(\text{O})\text{H}$, $-\text{R}^6\text{C}(\text{O})\text{R}^5$,
 $-\text{R}^6\text{C}(\text{O})\text{OH}$, $-\text{R}^6\text{C}(\text{O})\text{OR}^5$, $-\text{R}^6\text{C}(\text{O})\text{NH}_2$, $-\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{OC}(\text{O})\text{R}^5$,

$-\text{R}^6\text{OC}(\text{O})\text{NH}_2$, $-\text{R}^6\text{OC}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{OC}(\text{O})\text{Q}$ and YR^8 groups wherein Y is independently selected from $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{OC}(\text{O})-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{NHC}(\text{O})-$,

$-\text{NHSO}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{C}(\text{OH})\text{H}-$, $-\text{O}(\text{C}(\text{R}^9)_2)_q-$, $-\text{S}(\text{O})_m(\text{C}(\text{R}^9)_2)_q-$, $-\text{NH}(\text{C}(\text{R}^9)_2)_q-$,
 $-\text{NR}^{10}(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q\text{O}-$, $-(\text{C}(\text{R}^9)_2)_q\text{S}(\text{O})_m-$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}-$,
 $-(\text{C}(\text{R}^9)_2)_q\text{NR}^{10}-$, $-\text{C}\equiv\text{C}-$, *cis* and *trans* $-\text{CH}=\text{CH}-$ and cycloalkyl of 3 to 10 carbon atoms;

a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-\text{H}$, $-\text{J}$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{CN}$, $-\text{N}_3$,
 $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{H}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{R}^5$, $-\text{OR}^5$, $-\text{NHR}^5$, $-\text{Q}$,
 $-\text{S}(\text{O})_m\text{R}^5$, $-\text{NHSO}_2\text{R}^5$, $-\text{R}^6\text{OH}$, $-\text{R}^6\text{OR}^5$, $-\text{R}^6\text{NH}_2$, $-\text{R}^6\text{NHR}^5$, $-\text{R}^6\text{Q}$, $-\text{R}^6\text{SH}$, $-\text{R}^6\text{S}(\text{O})_m\text{R}^5$;

$-\text{NHR}^7\text{OH}$, $-\text{NHR}^7\text{OR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{OH}$, $-\text{N}(\text{R}^5)\text{R}^7\text{OR}^5$, $-\text{NHR}^7\text{NH}_2$, $-\text{NHR}^7\text{NHR}^5$, $-\text{NHR}^7\text{Q}$,
 $-\text{N}(\text{R}^5)\text{R}^7\text{NH}_2$, $-\text{N}(\text{R}^5)\text{R}^7\text{NHR}^5$, $-\text{N}(\text{R}^5)\text{R}^7\text{Q}$, $-\text{OR}^7\text{OH}$, $-\text{OR}^7\text{OR}^5$, $-\text{OR}^7\text{NH}_2$, $-\text{OR}^7\text{NHR}^5$;

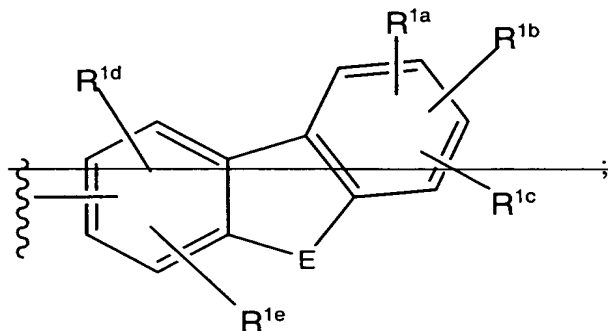
$-\text{OR}^7\text{Q}$, $-\text{OC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{R}^5$, $-\text{NHC}(\text{O})\text{NHR}^5$, $-\text{OR}^6\text{C}(\text{O})\text{R}^5$, $-\text{NHR}^6\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$,
 $-\text{C}(\text{O})\text{OR}^5$, $-\text{C}(\text{O})\text{NHR}^5$, $-\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{C}(\text{O})\text{H}$, $-\text{R}^6\text{C}(\text{O})\text{R}^5$, $-\text{R}^6\text{C}(\text{O})\text{OH}$, $-\text{R}^6\text{C}(\text{O})\text{OR}^5$;

$-\text{R}^6\text{C}(\text{O})\text{NH}_2$, $-\text{R}^6\text{C}(\text{O})\text{NHR}^5$, $-\text{R}^6\text{C}(\text{O})\text{Q}$, $-\text{R}^6\text{OC}(\text{O})\text{R}^5$, $-\text{R}^6\text{OC}(\text{O})\text{NH}_2$, $-\text{R}^6\text{OC}(\text{O})\text{NHR}^5$;

$-\text{R}^6\text{OC}(\text{O})\text{Q}$ and YR^8 groups wherein Y is independently selected from $-\text{C}(\text{O})-$,

$-\text{C}(\text{O})\text{O}-$, $-\text{OC}(\text{O})-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{NHC}(\text{O})-$, $-\text{NHSO}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{C}(\text{OH})\text{H}-$, $-\text{O}(\text{C}(\text{R}^9)_2)_q-$,
 $-\text{S}(\text{O})_m(\text{C}(\text{R}^9)_2)_q-$, $-\text{NH}(\text{C}(\text{R}^9)_2)_q-$, $-\text{NR}^{10}(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q-$, $-(\text{C}(\text{R}^9)_2)_q\text{O}-$,

$-(\text{C}(\text{R}^9)_2)_q\text{S}(\text{O})_m-$, $-(\text{C}(\text{R}^9)_2)_q\text{NH}-$, $-(\text{C}(\text{R}^9)_2)_q\text{NR}^{10}-$, $-\text{C}\equiv\text{C}-$, *cis* and *trans* $-\text{CH}=\text{CH}-$ and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula

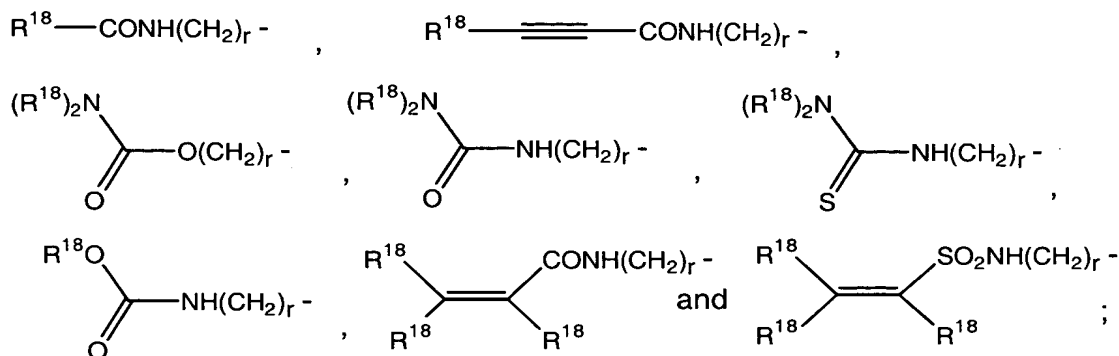


~~E is NH , NR^5 , O , S(O)_m , C(O) , CH_2 , CHR^5 or CR^5R^5 ;~~

Q is NR^5R^5 and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

~~R^{1a} , R^{1b} , R^{1c} , R^{1d} and R^{1e} are each, independently selected from H , J , NO_2 , NH_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , NHR^5 , Q , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^6OH , R^6OR^5 , R^6NH_2 , R^6NHR^5 , R^6Q , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, NHR^7OH , NHR^7OR^5 , $\text{N(R}^5\text{)R}^7\text{OH}$, $\text{N(R}^5\text{)R}^7\text{OR}^5$, NHR^7NH_2 , NHR^7NHR^5 , NHR^7Q , $\text{N(R}^5\text{)R}^7\text{NH}_2$, $\text{N(R}^5\text{)R}^7\text{NHR}^5$, $\text{N(R}^5\text{)R}^7\text{Q}$, OR^7OH , OR^7OR^5 , OR^7NH_2 , OR^7NHR^5 , OR^7Q , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 , C(O)NHR^5 , C(O)Q , $\text{R}^6\text{C(O)H}$, $\text{R}^6\text{C(O)R}^5$, $\text{R}^6\text{C(O)OH}$, $\text{R}^6\text{C(O)OR}^5$, $\text{R}^6\text{C(O)NH}_2$, $\text{R}^6\text{C(O)NHR}^5$, $\text{R}^6\text{C(O)Q}$, $\text{R}^6\text{OC(O)R}^5$, $\text{R}^6\text{OC(O)NH}_2$, $\text{R}^6\text{OC(O)NHR}^5$, aryl, CH_2aryl , NHaryl , Oaryl , $\text{S(O)}_m\text{aryl}$, R^{14} , OR^{14} , NHR^{14} and $\text{R}^6\text{OC(O)Q}$; R^{2a} , R^{2b} , and R^{2c} , are each, independently selected from H , aryl , CH_2aryl , Oaryl , $\text{S(O)}_m\text{aryl}$, J , NO_2 , OH , SH , CN , N_3 , COOH , CONH_2 , NHC(O)NH_2 , C(O)H , CF_3 , OCF_3 , R^5 , OR^5 , $\text{S(O)}_m\text{R}^5$, NHSO_2R^5 , R^{11} , OR^{11} , R^6OH , R^6OR^5 , R^6SH , $\text{R}^6\text{S(O)}_m\text{R}^5$, OR^7OH , OR^7OR^5 , OC(O)R^5 , NHC(O)R^5 , NHC(O)NHR^5 , $\text{OR}^6\text{C(O)R}^5$, $\text{NHR}^6\text{C(O)R}^5$, C(O)R^5 , C(O)OR^5 ,~~

-C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OR⁵, -R⁶C(O)NH₂,
 -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q,
 -G-(C(R⁹)₂)_p-R¹², -(C(R⁹)₂)_q-R¹²,



G is -NH-, -NR¹⁰-, -O- or -S(O)_m-;

R³ is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰, -(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and -G(C(R⁹)₂)_pOH; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R⁹)₂)_qOH, -(C(R⁹)₂)_qOR¹⁰, -(C(R⁹)₂)_qNHR¹⁰,

-(C(R⁹)₂)_qJ, -(C(R⁹)₂)_qNH₂, -(C(R⁹)₂)_rH, -G(C(R⁹)₂)_pOR¹⁰, -G(C(R⁹)₂)_pR¹², and

-G(C(R⁹)₂)_pOH; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein

the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^4 is selected from $-(C(R^9)_2)_rH$, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$,

$-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$,

$-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$,

$-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and

$-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$,

$-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$,

$-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring

system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, $-CHO$, 1,3-dioxolane, $-NO_2$, $-CN$, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

R^5 is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^6 is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R^7 is a divalent alkyl group of 2 to 6 carbon atoms;

R^8 is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-R^6R^{12}$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-H$, $-aryl$, $-CH_2aryl$, $-NHaryl$, $-Oaryl$, $-S(O)_maryl$, $-J$, $-NO_2$, $-NH_2$, $-OH$, $-SH$, $-CN$, $-N_3$, $-COOH$, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, $-Q$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$,

$-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$,
 $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$,
 $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$,
 $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-R^6R^{12}$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$,
 $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$,
 $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$,
 $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$; a bicyclic heteroaryl ring system having 8 to 20
atoms containing 1 to 4 heteroatoms which may be the same or different selected
from N, O and S wherein the bicyclic heteroaryl ring system may be optionally
substituted with 1 to 4 substituents which may be the same or different selected from
-H, -aryl, $-CH_2$ aryl, -NHaryl, -Oaryl, $-S(O)_m$ aryl, -J, $-NO_2$, $-NH_2$, -OH, -SH, -CN, $-N_3$,
-COOH, $-CONH_2$, $-NHC(O)NH_2$, $-C(O)H$, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-NHR^5$, -Q,
 $-S(O)_mR^5$, $-NH SO_2R^5$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$,
 $-R^6SH$, $-R^6R^{12}$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$,
 $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$,
 $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$,
 $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q$, $-R^6C(O)H$,
 $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$,
 $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and $-R^6OC(O)Q$;

R^9 is independently -H, -F or $-R^5$;

R^{10} is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R^{11} is a cycloalkyl group of 3 to 10 carbon atoms;

R^{12} is $-N(O)_n$, $R^{13}R^{14}$ or $-N^+(R^{10}R^{13}R^{14})J^-$;

provided that when R^{12} is $N(O)_n$ $R^{13}R^{14}$ and n is 1, R^{13} or R^{14} are not H;

R^{13} and R^{14} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}-R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}-R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}-R^{15}$, $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, $-(C(R^9)_2)_pS(O)_mR^{16}$, $-(C(R^9)_2)_pCO_2R^{16}$, $-(C(R^9)_2)_pC(O)NHR^{16}$ and

$-(C(R^9)_2)_pC(O)R^{15}$; further provided that R^{13} and R^{14} may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}R^{15}$, $-(C(R^9)_2)_q\text{heteroaryl}R^{15}$, $-(C(R^9)_2)_q\text{heterocyclyl}R^{15}$, $-(C(R^9)_2)_qCO_2R^{16}$, $-(C(R^9)_2)_qC(O)NHR^{16}$, and $-(C(R^9)_2)_qC(O)R^{15}$; or optionally substituted on carbon by -F, $-(C(R^7)_2)_qOR^{16}$, $-(C(R^7)_2)_qNR^{16}R^{17}$, and $-(C(R^9)_2)_qS(O)_mR^{16}$; or optionally substituted on nitrogen by $-(C(R^9)_2)_pOR^{16}$, $-(C(R^9)_2)_pNR^{16}R^{17}$, and $-(C(R^9)_2)_pS(O)_mR^{16}$;

R^{15} is independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNH_2$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qR^{10}$, $-(C(R^9)_2)_qS(O)_mR^{10}$, $-(C(R^9)_2)_qCO_2R^{10}$, $-(C(R^9)_2)_qCONHR^{10}$, $-(C(R^9)_2)_qCONR^{10}R^{10}$, $-(C(R^9)_2)_qCOR^{10}$, $-(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

R^{16} and R^{17} are independently selected from a group consisting of -H, $-R^5$, $-R^{11}$, $-(C(R^9)_2)_q\text{aryl}$, $-(C(R^9)_2)_q\text{heteroaryl}$, $-(C(R^9)_2)_q\text{heterocyclyl}$, $-(C(R^9)_2)_pOH$, $-(C(R^9)_2)_pOR^{10}$, $-(C(R^9)_2)_pNH_2$, $-(C(R^9)_2)_pNHR^{10}$, $-(C(R^9)_2)_pNR^{10}R^{10}$, $-(C(R^9)_2)_pS(O)_mR^{10}$, $-(C(R^9)_2)_pCO_2R^{10}$, $-(C(R^9)_2)_pCONHR^{10}$, $-(C(R^9)_2)_pCONR^{10}R^{10}$, $-(C(R^9)_2)_pCOR^{10}$, $-(C(R^9)_2)_pCO_2H$, and $-(C(R^9)_2)_pCONH_2$;

R^{18} is independently selected from the group consisting of -H, -aryl, $-R^5$, $-R^6NH_2$, $-R^6NHR^5$ and $-R^6Q$;

provided that, the 6-position is substituted when T and Z are carbon, A is absent, r is 0 and R⁴ is $-(C(R^9)_2)_rH$, then,

- a. ~~R^3 is not unsubstituted thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or alkynyl; or~~
- b. ~~R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_{27})_qOH$, or $-(C(R^9)_{27})_qOR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- c. ~~R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_{27})_6R^{12}$ and R^{12} is $NR^{13}R^{14}$;~~

further provided that, when T and Z are carbon, A is absent and R^4 is phenyl, then,

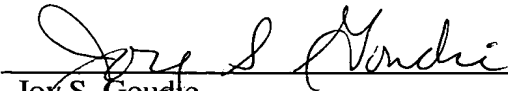
- a. ~~R^4 is not substituted by NO_2 , CN , CO_2H , $CONH_2$, CO_2R^{10} , $CONHR^{10}$, $-(C(R^9)_{27})_qOH$, $-(C(R^9)_{27})_qOR^{10}$, $-(C(R^9)_{27})_qNHR^{10}$, $-(C(R^9)_{27})_qJ$ or $-(C(R^9)_{27})_qNH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and~~
- b. ~~R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^9)_{27})_6R^{12}$ and s is 0 and R^{12} is $NR^{13}R^{14}$;~~

additionally provided that, when T and Z are carbon, then,

- a. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and~~
- b. ~~carbon-8 is not substituted by OH , OR^{10} , SR^{10} , or OR^{11} when X is O and carbon-5 is substituted by aryl or heteroaryl;~~

further provided that when either T or Z are N, then R^{26} is absent; or a pharmaceutically acceptable salt thereof.

Applicants believe that the present application is in condition for allowance and respectfully request that the Examiner enter the amendment and allow the application. Favorable treatment of the application is earnestly solicited.


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